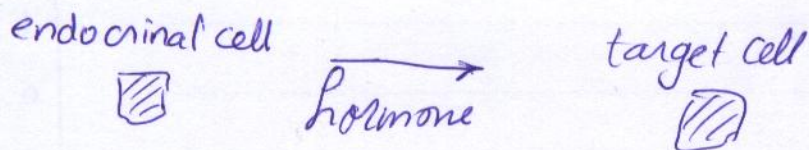


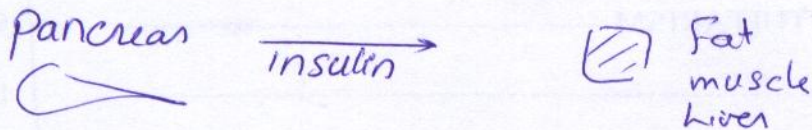
endocrine
 clinical / (سجل) /
 spot diagnosis

Introduction to Endocrine

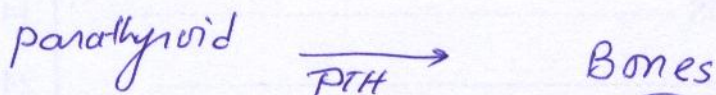
Hormones = Hormone



eg

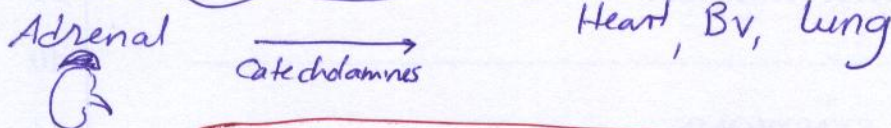


eg



→ hormone: chemical messenger produced from endocrinal cell to act on distant target cell distant from site of production

eg



* TRH

* TSH = thyrotropin

* Hypothalamo-pituitary axis

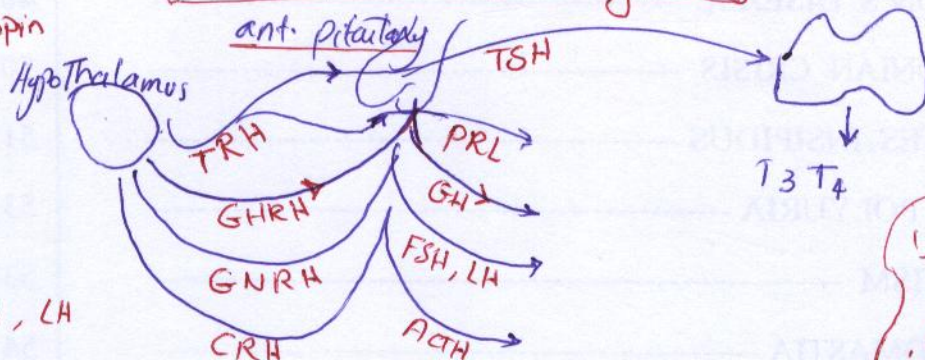
* GHRH → GH

* GnRH → FSH, LH

* CRH = Corticotropin releasing hormone

→ ACTH = Adrenocorticotrophic hormone (on zona fasciculata)

Introduction to thyroid



محور الغدة الكظرية

axis
 • Pancreas
 • parathyroid

① Trapping [uptake]

2 forms in blood

* Thyroxin Binding Globulin (TBG)

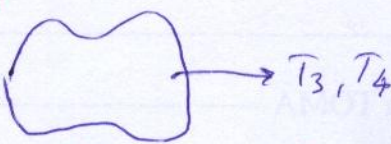
* free

free + TBG = Total

free = 0.1% of total
 TBG مفيد مقارنة مع
 لانه free

Iodine

Blood



- T4 > T3 in blood
 - T3 > T4 in potentiality

② Binding = I + Tyrosine = MIT

2I + Tyrosine = DIT

③ Coupling = MIT + DIT = T3 triiodothyronine

DIT + DIT = T4 Tetraiodothyronine

④ storage: T3 & T4 + globulin ⇒ Thyroglobulin

⑤ Release:

splitting → by Protease

higher control of TSH

(eg)

free T3, T4 + Globulin

VISIT...

LANZAROTE
Caliente.COM

↓ growth, Cholesterol ↓, G ↓, Anemia ← T_3, T_4 يقل
 Cholesterol ↓, GT ↑, flushed ← T_3, T_4 زياد

MYXOEDEMA

DEFINITION

- It is a SEVERE form of hypothyroidism.

ETIOLOGY

I. PRIMARY MYXOEDEMA

- The problem is in the thyroid gland itself: "ACQUIRED" or "CONGENITAL"

A) ACQUIRED HYPOTHYROIDISM

1. Inflammation:

"Hashimoto's thyroiditis"

- Autoimmune disease.
- Associated with: thyroid antibodies in 100 % of the cases.
- Associated with: other autoimmune diseases, e.g. PA, SLE, RA, ITP.

2. Idiopathic:

"The most common cause"

- Autoimmune disease. [Atrophic thyroiditis]
- Associated with: thyroid antibodies in 80 % of the cases.
- Associated with: other autoimmune diseases, e.g. PA, SLE, RA, ITP.
- Associated with: thyroid atrophy. Atrophic thyroiditis
- It is probably: the end-stage of Hashimoto's thyroiditis.

3. Iatrogenic:

- Thyroidectomy, excessive Radio-iodine therapy, prolonged use of antithyroid drugs.

4. Irradiation:

- Irradiation for lymphoma may damage the thyroid gland.

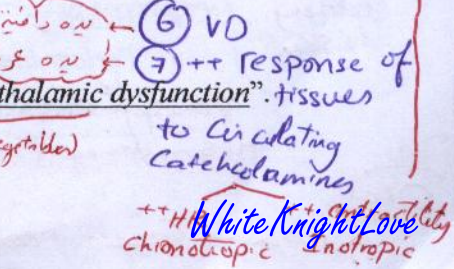
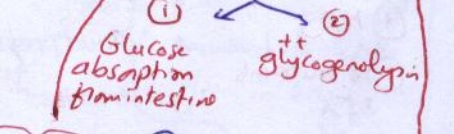
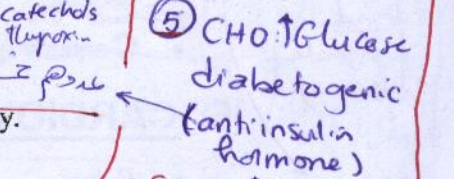
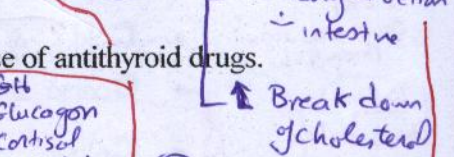
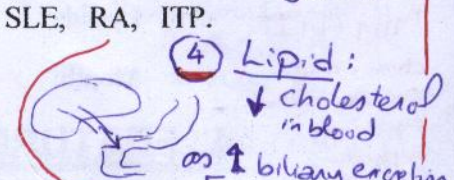
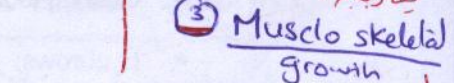
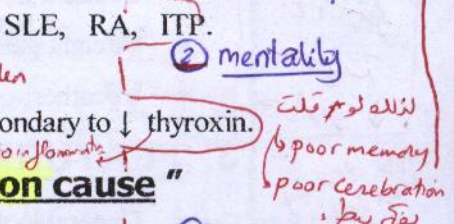
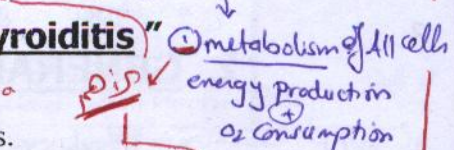
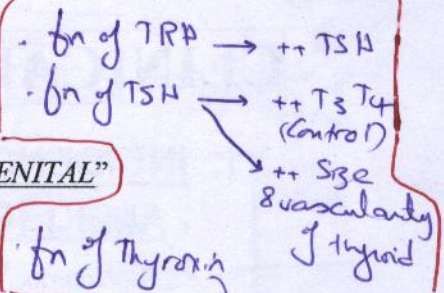
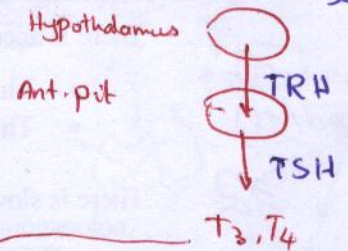
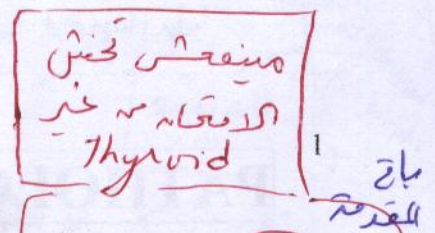
5. Iodine deficiency:

- Endemic myxoedema occurs due to prolonged iodine deficiency.

B) CONGENITAL HYPOTHYROIDISM.

II. SECONDARY MYXOEDEMA

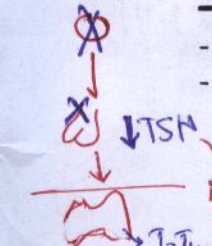
- The problem is not in the thyroid gland itself.
- The problem is suprathyroid: "Pituitary dysfunction" OR "Hypothalamic dysfunction".



Hashimoto MCQ

في رايي
 اقول انهم مرض
 في رايي
 الكافي اني
 سات
 hashimoto
 وقتي
 long standing
 fibrous atrophy

Oral
 Amiodarone
 Lithium
 (antipsychotic)



7 RBC
 ++ Erythropoietin

8 Carotene (vegetables)
 vit A

6 VD
 7 ++ response of
 to circulating
 catecholamines
 ++ Hb activity
 chronotropic inotropic

↓ thyroid → ↓ enzymes activity (w/ metabolic MPS) [↓ catabolism]
 ↓ thyroid → ↓ Excretion of MPS

PATHOLOGY

- There is accumulation of **mucopolysaccharide** in the subcutaneous tissue, leading to:

- Thickening of the skin: nonpitting oedema "**myxoedema**". as
- Thickening of the facial features.

any site (extra cellular)
mainly S.C.

CLINICAL PICTURE

1. INCIDENCE

- Age: 30 - 50 years. (auto immune) < 100% Hashimoto 80% atrophic Abs
- Sex: more common in FEMALES.
- Onset: gradual with delayed symptoms.

2. GENERAL FEATURES

- Weakness**, fatigue. → ↓ Energy production
- Weight gain**, up to obesity, slow movement. → ① ↓ metabolism & ② ↑ deposition of MPS
- Weather**: Intolerance to cold, + hypothermia. → ① ↓ Energy ② obese

3. FEATURES OF THE FACE

- General look**: face is **expressionless** & **bloated**. due to ↓ Energy production in swollen (MPS in cheeks)
- Eyebrows**: sparse with loss of the outer third. → poor response & poor
- Eyelids**: puffy. → hair follicles
- Mouth**: thickened lips & thickened tongue.

4. FEATURES OF THE SKIN

- Cold**, & dry: ↓ heat production (↓ metabolism) → ↓ VC → ↓ HF if occurred → redistribution of blood to heart & brain on exposure of skin
- Coarse** & thickened: decreased sweating → nonpitting oedema "**myxoedema**"
- Colour**: pale due to anemia & yellowish due to deposition of carotene.
- Contains sparse** & brittle hair. → eye brows

5. CARDIOVASCULAR FEATURES

- Pulse**: sinus bradycardia.
- Blood pressure**: secondary hypertension.
- Arteries**: atherosclerosis which may cause CAD.
- Heart**: cardiomegaly due to CM which may end in HF. impending HF
- Pericardium**: pericardial effusion, & may be pleural effusion & ascites.

Polysystoles

MPS → damage of caps → ↑ permeability

Oral

lips → Causes of carotenemia < 2

GRF

anemia

Macrocytic { 1 ↓ abs. FA/B₁₂
2 ↑ cholesterol
3 associated P.A.
Normocytic (↓ erythropoietin)
Microcytic (Fe²⁺) < menorrhagia malabsorption

White Knight Love

constipation
malabsorption
slow mentality

Spot diagnosis
كل شيء
رأى زايه
فعا
ما تدرش عليه
الوش ضيق
والجانب
تسلم على نفسك
والله اعلم

خا السرير
تخينة
حرارة

MPS destroys hair follicles

D.D.
Puffy Eyes
chronic cough
SVC obstruction
eye causes
nephrotic & CRF
cavernous sinus thrombosis

D.D.
loss outer third
Myxoedema leprosy

Mask face
1 Parkinsonism
2 scleroderma
3 Bilateral facial N.
4 Myxoedema
5 Myasthenia

acromegaly
↑ GH

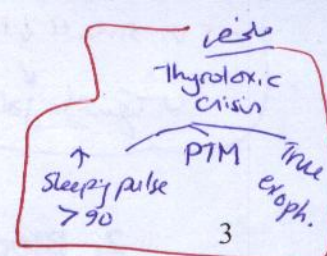
GRF
1 - ↓ metabolism
2 - ↓ response to catecholamines
3 - MPS destroys sweat gland sebaceous glands

Jaundice
1 eye
2 urine
3 stool
abnormal = jaundice

Cerebral → stroke
Peripheral → ischemia

B.P. ↑ : ↑ cholesterol → Atherosclerosis

GRF H.F. in Myxedema: ① DCM (infiltrated by MPS)
② HTN (2nd common cause of HF)
③ CAD (1st common cause of HF)
④ ↓ inotropism



6. GENITAL FEATURES

- Galactorrhoea & Menorrhagia: in females.
- Gynecomastia: in males.

7. GIT FEATURES

- Slow motility → constipation OR myxoedema megacolon.
- Slow absorption → malabsorption.

8. NEUROLOGICAL FEATURES

الغثاسنة
Constipation
malabs. لا لو حصل
Diarrhea

relative ↓ Estrogen

NEUROLOGICAL FEATURES OF MYXOEDEMA

- M**ental impairment: poor memory, ^{Poor cerebration} slow thinking, somnolence.
- M**yxoeedema madness: psychosis, depression. → lazy
- M**yxoeedema coma.
- M**yopathy & peripheral neuropathy. → (disturbed neurotransmitter)
- M**ucopolysaccharide accumulation:
 - In the vocal cords → hoarseness of voice.
 - In the internal ear → impaired hearing.
 - In the flexor retinaculum → carpal tunnel syndrome.
- Deep reflexes: delayed relaxation of deep reflexes. = sustained deep reflex

9. FEATURES OF THE THYROID GLAND

- Enlarged or there is scar of thyroidectomy. ^{hashimoto} ^{iatrogenic}

10. MYXOEDEMA COMA

- Age: more common in old patients.
- Precipitating factors: exposure to severe cold, infections.
- Clinical picture: confusion, then coma with:
 - Hypothermia. ^{no Energy}
 - Hypoventilation. ^[Resp failure]
 - Hypoglycemia.
 - Heart failure.

INVESTIGATIONS

1. Thyroid function tests:

- T3 & T4 (total & free): decreased.
- TSH: increased in primary & decreased in secondary.
- Thyroid radioactive I uptake: decreased.

Increased TSH in primary myxoedema is the most important investigation.

(MCO) Normal levels of TSH will exclude Hypothyroidism (✓)
Normal levels of T3, T4 do not exclude White Knight Love

local
S.O.
أسفوي
as emergency

↓ metabolism
J.R.C
Resp. Ms

as both Contract & Relaxation need Energy

استهلاك
آخر سوية
Energy
عند
فشل الخ
تأخر

marked depletion of E. in brain cells
فشل في غيبوبة

قدرة
في الغدة
التي تفرز
I2

as v. small $\downarrow T_3 T_4 \rightarrow$ 1 TSH markedly
الحال الجيد $\rightarrow$ الحال الجيد

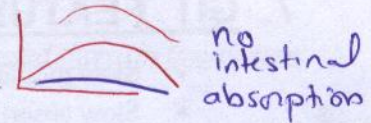
لذلك تزداد TSH بغير علة
في حين ان $T_3 T_4$ طبيعي
لذلك انخفضت افعاله حاصلة الغوشت
4 $T_3 T_4$ و TSH و TSH هو الارتفاع

2. Blood picture:

- Normocytic anemia: due to BM depression.
- Microcytic anemia: due to iron loss in menorrhagia.
- Macrocytic anemia: due to associated pernicious anemia.

3. Biochemical changes:

- Serum cholesterol: high.
- Serum glucose: flat glucose tolerance curve.
- Serology: thyroid antibodies in Hashimoto's & Idiopathic thyroiditis.
- SGOT & CPK: not specific for myopathy of myxedema. may be elevated due to myopathy.



4. ECG:

- Rhythm: -ve chrono Sinus bradycardia.
- Voltage: -ve Ino Low voltage.
- T wave: Flat or inverted T wave. V. non specific

- ① -ve inotropism
- ② pericardial effusion
- ③ DCM
- ④ MPS

ECG: 1-1-1

DIFFERENTIAL DIAGNOSIS

1. Nephrotic syndrome.
2. Chronic renal failure.
3. Weight gain & obesity.
4. Anemia.
5. Depression.
6. Coma.
7. Polyserositis.
8. Differentiate between primary & secondary myxoedema.

clinical features of Hypothyroidism

$\uparrow TSH$ & $\downarrow T_3 T_4$

& discovered accidentally
follow up every 6M till clinically

V. small doses thyroxin 25-50 ug/d
replacement to delay development of hypothyroidism clinically

TREATMENT

"life long"

1. L - thyroxin:

- Start by: 50 ug / day.
- Increase the dose every one month by: 50 ug / day.
- Average maintenance dose: 200 ug / day.
- In old people & in patients with CAD: start by a lower dose (25 ug / day), & the dose is increased very gradually to avoid precipitation of angina & HF.
- Improvement is judged clinically, & by normalization of ECG & cholesterol.

not give 200 from start as +ve in ECG already n. low
HF or angina

2. Treatment of myxoedema coma:

+ Case of comatized

- For Hypothyroidism: IV Hydrocortisone 100 mg / 8 hours.
- For Hypothermia: Gradual rewarming.
- For Hypoventilation: Adequate oxygenation & ventilatory support.
- For Hypoglycemia: Dextrose infusion.
- For Heart failure: ttt of HF. eg digitalis, diuretic

Stroke
IV T_4 500 ug single dose

If T_3 & cortisol $\rightarrow$ Sudden severe stimulation of metabolism (stress) of all tissues $\rightarrow$ Conservation of Adrenal reserve

3- Ht of subclinical hypothyroidism:

Acute Addison
White Knight Love



DISORDERS OF THE PITUITARY GLAND

I. DISORDERS OF THE ANTERIOR PITUITARY

1. Hyperpituitarism:

Handwritten notes: "Control of TRH" and "دائماً به" (Always to).

Excess secretion of	Disease
GH	Gigantism & Acromegaly
Prolactin	Galactorrhea
ACTH	Cushing's syndrome disease
TSH	Hyperthyroidism
Gonadotropins	Precocious puberty
MSH melanocyte stimulating Hr.	Hyperpigmentation

Handwritten notes: "syndrome of Addison's disease" and "Adrenal" with a drawing of an adrenal gland.

2. Hypopituitarism:

a) In childhood:

Handwritten note: "↓ GH"

- Pituitary dwarfism (Levi-Lorain syndrome).
- Frolich's syndrome.
- Laurance Moon Biedle syndrome.

Handwritten note: "dwarfism"

b) In adults:

Handwritten note: "نادر خط واحد بس يتصل" (Rare, only one line connects).

- Isolated hormonal deficiency:
 - Decreased ACTH → Pituitary Addison's disease.
 - Decreased TSH → Pituitary myxoedema.

Handwritten note: "النشهر كله يتصل" (The whole pituitary connects).

- Pan Hypopituitarism: (Simmond's disease).
Sheehan's

II. DISORDERS OF THE POSTERIOR PITUITARY

- Decreased ADH → Diabetes insipidus..
- Increased ADH → SIADH.

GIGANTASIM

ETIOLOGY

- Excessive secretion of GH "before fusion of the epiphysis" due to:

- Pituitary hyperplasia: common.
- Pituitary adenoma: rare.

Affecting
Acidophil
cells
GH بنه

Puberty

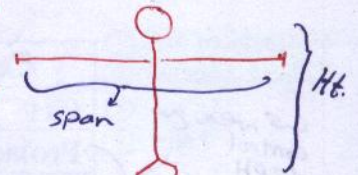
hyperplasia: قاعدة
if long standing
Tumor: قطب

لا ياتي نظري
ولا ياتي clinical
DD. of
Long stature
tall

CLINICAL PICTURE

A) ENDOCRINAL MANIFESTATIONS

1. Disproportionate gigantism: span > height.
2. Later on: features of acromegaly occur.
3. Very late: fatigue & weakness occur due to pituitary insufficiency.



Elong standing
hyperfunction
↓
exhaustion of pit
tissue
or long standing
adenoma
↓
enlarges & destroy
the gland

B) NEUROLOGICAL MANIFESTATIONS

- Refer to "Brain tumours" in Neurology.

"pressure manifestations"

INVESTIGATIONS

- See investigations of Acromegaly.

- 1 - ant
- 2 - post
- 3 - lat
- 4 - above

DIFFERENTIAL DIAGNOSIS

- From other causes of: "TALL STATURE":

1. Familial & racial: proportionate gigantism. (span = height)
2. Primary hypogonadism: Disproportionate gigantism + feminine characters.
3. Marfan's syndrome: Aortic regurge, Mitral Regurge. (MVP)
Dislocation of the lens, Dislocation of the joints.
High arched palate, Arachnodactyly.



↓ sex hormones
(sex hr. needed
for epiphyseal closure)

TREATMENT

- See treatment of Acromegaly.

ACROMEGALY

clinical

ETIOLOGY

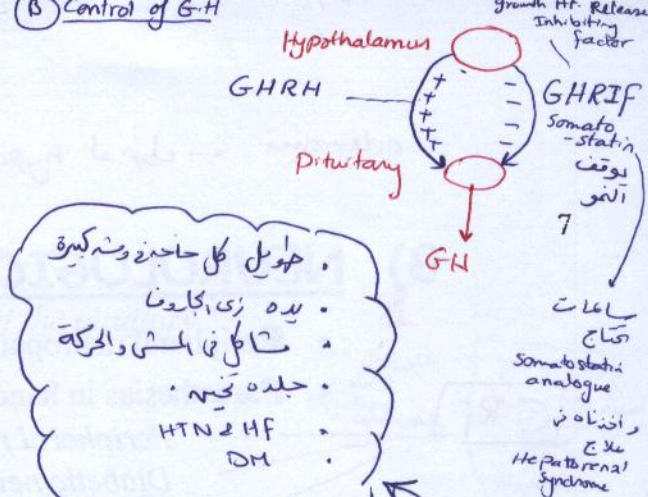
- Excessive secretion of GH "after fusion of the epiphysis" due to:

- Pituitary adenoma: common.
- Pituitary hyperplasia: rare.

Acidophils

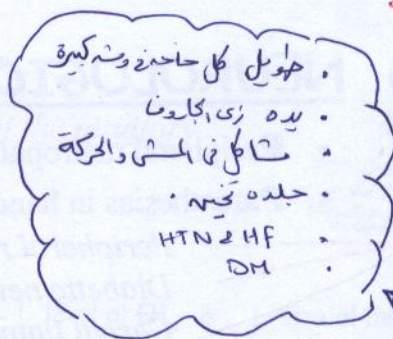
acromegaly

- A) Action of G.H**
1. PTH: anabolic (body building: growth & develop of all tissues)
 2. ↑ Ca ↑ Ph: ↑ intestinal absorption (تزيد الامتصاص المعوي)
 3. Diabetogenic ↑ G: ↑ Glucoseogenesis (تزيد إنتاج الجلوكوز)
- MS Bone skin viscera



CLINICAL PICTURE

- Age: 20 – 40 years. ♂ = ♀
- Onset: gradual.
- Course: slowly progressive.



A) ENDOCRINAL MANIFESTATIONS

Spot Diagnosis

1. Head & face:

وصف من كوين
"Ape-like face"

- Big skull with elongated face.
 - Big ears, Big nose, Big lips, Big tongue.
 - Prognathism + separation of the teeth. — as jaw enlarges → widened alveolar spaces
 - Prominent frontal bosses & prominent supraprbitar ridges.
- Protruded mandible due to growth
X-ray lat view

2. Hands:

"Spade-like hands"

أي الجاوف

- Big hands with blunt fingers.

3. Skeletal affection:

- Osteoarthritis may occur. degenerated
- Ligament laxity = instable joint

4. Skin affection:

- Thick, wrinkled, greasy. — hypertrophied sebaceous glands
- due to overgrowth of Periarticular C.T. → stretch of ligaments for long time → lax

5. Organ enlargement:

- Hepatosplenomegaly.
- Heart enlargement (with Cardiomyopathy) → HF. — due to DCM
- Hypertrophy of the wall of the blood vessels → Hypertension. — HTN
- Hypertrophy of the larynx → Hoarseness of voice.

6. Associated endocrinal disturbances:

- Diabetes mellitus: may occur in 30 % of the cases. — diabetogenic effect
- Galactorrhea: may occur. — adenoma of pit. → secrete PRL

7. Muscle affection:

- Early: increased muscle power.
- Late: decreased muscle power & MYOPATHY.

Muscle overgrowth → outgrows its blood supply
relative ischemia ← & already B.V. thickened
White Knight Love

دفعاً لدم
تقيس الضغط
بالد
acromegaly

adenoma ← Adenoma غالباً Adenoma وحسب لـ hyperplasia لو طول ←

8

B) NEUROLOGICAL MANIFESTATIONS

- **Peripheral neuropathy.** ↑ Growth of interstitial tissue of nerve → thickened
- **Parasthesias in hands & feet may occur due to:**

GRF

- Peripheral neuropathy.
- Diabetic neuropathy. 30%
- Carpal tunnel syndrome. Entrapment neuropathy

- 1 hypertrophy of nerves →
- 2 " of bone
- 3 " of retractor

delayed conduction
تأخر في التوصيل

- **Pressure manifestations:**
- Refer to "Brain tumours" in Neurology.

أشهر
أكثر دواعي
عنه دى ن

INVESTIGATIONS

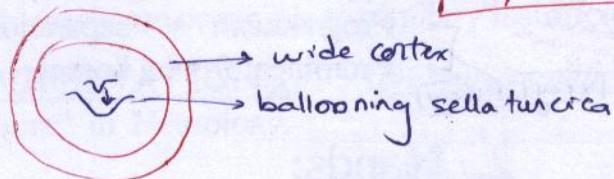
I. IMAGING

1. X-ray:

a) Skull:

- Thick cortex.
- Wide frontal sinuses.
- Prognathism + separation of the teeth.
- Sellar changes: enlargement of the sella turcica.

Lat view



b) Hands:

- Phalanges: Broadening of the phalanges.
- Terminal phalanges: Tufting of the terminal phalanges (mushroom-like).

Soft tissue is v. prominent



أشهر الأمراض
metastasi
Acromegaly
Thalassemia
RA
Acromegaly

2. CT & MRI of the skull:

- For accurate diagnosis of pituitary tumours.

للتنقية بجاذب واحدة
في مفصل
Joint space
if preserved → Acromegaly

II. HORMONES

1. GH level in the serum:

- Increased (normally: < 5 ng/ml in adults).

GH

2. Glucose suppression test:

- IV glucose fails to decrease GH level.

IV Glucose → ↑ glucose in blood

3. Prolactin level in the serum:

- Increased in 30 % of the cases.

دواء
Pit. بقل إفراز هرمون النمو
-ve feed

III. BLOOD CHEMISTRY:

- Increased Ca, Increased Phosphates, Increased Glucose.

30 %

TREATMENT

1. Surgical ttt:

- Trans-sphenoidal.
- Trans-frontal

"Removal of the pituitary"

2. Medical ttt:

- Bromocriptine (30 mg / day): $\downarrow$ level of GH & $\downarrow$ size of the tumour.
- Synthetic somatostatin (100 mcg / 8 h): *the drug of choice.*

3. Irradiation of the pituitary:

- If surgical ttt is contraindicated
- If medical ttt gives no response.

4. Symptomatic ttt:

- e.g. for DM & for Hypertension. & Hf

anti diabetic

anti HTN

دوپامين
في علاج
Hepatic
encephalopathy

dopamine
also
anti parkinsonal

migraine &
dopamine
antagonist

SS = octreotide
 $\downarrow$ GH release
في علاج
Hf

ACEI
ARBs

PAN HYPOPITUITARISM

(Simmond's disease)

ETIOLOGY

1. Post-partum hemorrhage "Sheehan's syndrome": *the most common cause*

- Post-partum hemorrhage $\rightarrow$ VC & increased clotting tendency $\rightarrow$ thrombosis of the pituitary vessels $\rightarrow$ pituitary infarction.

2. Pituitary tumours.

chromophobe adenoma
craniopharyngioma

3. Pituitary removal by surgery or pituitary irradiation.

$\rightarrow$ can't proper replacement

CLINICAL PICTURE

I. EARLY FEATURES

- Insidious onset of:

II. DEFICIENCY FEATURES

1. Gonadal deficiency:

a) In females:

$\downarrow$ PRL

$\downarrow$ FSH, LH

- Failure to establish lactation after delivery or infertility.
- Atrophy of the breasts, Amenorrhea.
- Loss of libido, Loss of pubic & axillary hair.

b) In males:

- Impotence.
- Loss of libido, Loss of pubic & axillary hair.

PRL TSH GH FSH ACTH
LH

ϕ more common

Triad
weakness & apathy & wt. loss

$\downarrow$ ACTH

$\downarrow$ TSH
($\downarrow$ T₃ T₄)
(myxoedema)

$\downarrow$ GH if
wt loss $\leftarrow$ $\downarrow$ GH $\rightarrow$ $\downarrow$ TSH
wt gain $\leftarrow$ $\downarrow$ GH $\leftarrow$ $\downarrow$ TSH
no change $\leftarrow$ $\downarrow$ GH = $\downarrow$ TSH

breast
& hair
normal
= Anorexia
nervosa

Oral
Adrenal failure
فشل الغدة الكظرية

↓ TSH

↓ ACTH

2. Thyroidal deficiency:

- Clinical features of myxoedema.

"Secondary myxoedema"

عندما يكون هناك قصور في الغدة الدرقية
توضيح: إذا كان هناك قصور في الغدة الدرقية
فإنه يسمى Myxoedema
S.Q. → اشترط

3. Adrenocortical insufficiency:

"Secondary adrenal failure"

- Clinical features of Addison's disease,

BUT:

- 1 - Hyperpigmentation: is absent.
- 2 - Hypotension: is not severe due to continued release of aldosterone.

ACTH

adrenal cortex
ery adrenal failure

4. Pressure manifestations:

- In case of pituitary tumours.

لو كان هناك ورم في الغدة النخامية

Addison's disease
فشل الغدة الكظرية

II. LATE FEATURES

COMA may occur in late stages due to:

- Hypothermia.
- Hypoglycemia.

(↓ TSH) → Myxedema Coma

↓ TSH, ↓ GH, ↓ ACTH → Hypoglycemic Coma

INVESTIGATIONS

1. IMAGING

- X-ray sella turcica.
- CT & MRI of the brain.

2. HORMONES

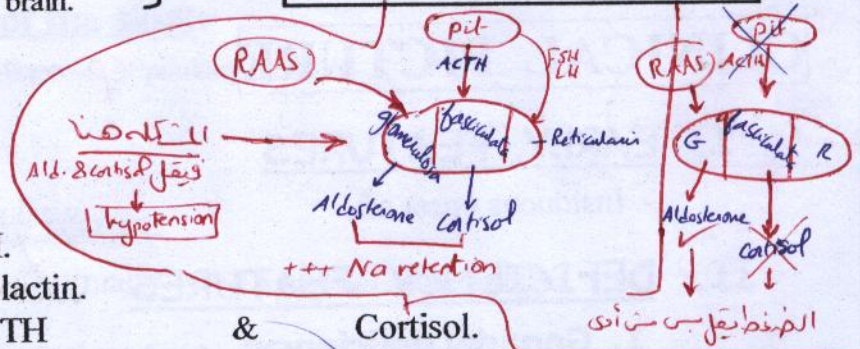
A) ASSAY:

- Decreased GH.
 - Decreased Prolactin.
 - Decreased ACTH
 - Decreased TSH
 - Decreased Gonadotrophins
- & Cortisol.
& T3 & T4.
& Sex hormones.

B) COMBINED INSULIN TOLERANCE TEST:

- Give: IV INSULIN, followed by TRH & GnRH.
- Normally: marked ↑ in GH, ACTH, TSH, Prolactin, FSH, LH.
- In Pan hypopituitarism: no increase in these hormones.

Evidence of Pituitary tumour



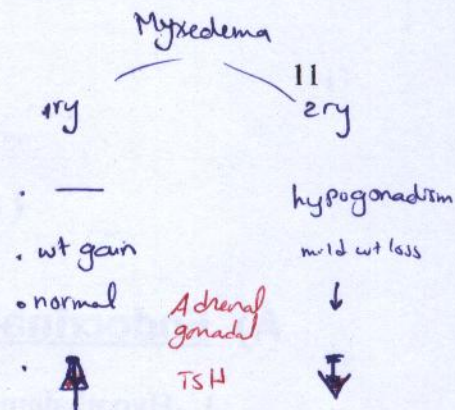
selective ↓
TSH cortisol gonadal

DIFFERENTIAL DIAGNOSIS

1. Primary myxoedema:

"Thyroid myxoedema"

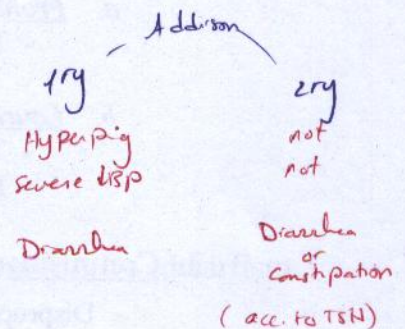
- Features of myxoedema.
- Hypogonadism: absent.
- Body weight: markedly increased.
- Investigations:
 - Gonadal & Adrenal functions: normal.
 - TSH: high.



2. Primary adrenal failure:

"Addison's disease"

- Features of Addison's disease.
- Hyperpigmentation & Hypotension.
- Diarrhoea.
- Investigations:
 - Gonadal & Thyroid functions: normal.
 - ACTH: high.
 - ACTH administration: no effect.



3. Anorexia nervosa:

- It usually occurs in: YOUNG WOMEN.
- ANOREXIA + marked loss of weight.
- AMENORRHEA + normal axillary & pubic hair.
- Breasts are well developed.
- Thyroxin & cortisol levels are NORMAL.

الفقرات
Sheehan

4. Primary hypogonadism in males:

- Features of hypogonadism.
 - Disproportionate gigantism: if the condition starts in childhood.
 - Thyroxin & cortisol levels are NORMAL.
- Handwritten notes: "↓ sex hr. w is needed to close ep.phys." (circled), "heart size" (circled).

TREATMENT

1. Treatment of the cause, if possible.

الفقرات

2. Hydrocortisone: 30 mg / day.

3. Thyroxin:

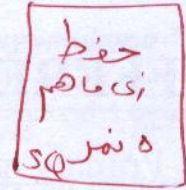
- It should be given after hydrocortisone, to avoid acute adrenal insufficiency.
- It should be given in a small dose, followed by very gradual increase of the dose.

4. Gonadal hormones:

- In females: diethylstilbestrol.
- In males: methyl testosterone.

DWARFISM

(Stunted growth - - Short stature)



A) Endocrinal diseases

1. Hypothalamic syndromes:

a. Frohlich's syndrome:

- Trunkal obesity, hypogonadism, genu-valgum.

b. Laurance Moon Biedle syndrome:

- Trunkal obesity, hypogonadism, genu-valgum.
- Polydactyly, mental retardation, retinitis pigmentosa.

2. Cretinism:

- Disproportionate dwarfism + features of cretinism.

3. Pituitary dwarfism

“ Levi-Lorain syndrome ”

- Proportionate dwarfism + hypogonadism.

4. Precocious puberty:

- Increased secretion of sex hormones causes premature fusion of the epiphysis.

5. IDDM.

B) Severe chronic illness during childhood

1. Cardiac: Congenital, Rheumatic valvular.

2. Chest: Cystic fibrosis, Severe bronchial asthma.

3. Liver: Lipid & glycogen storage disease, Veno-occlusive disease.

4. GIT: Malnutrition, Malabsorption.

5. Renal: Chronic renal failure.

6. Blood: Chronic severe anemia.

7. Chronic infections: e.g. TB.

C) Skeletal causes

1. Achondroplasia:

- Limbs: Short.
- Trunk: Normal.

2. Osteochondrodystrophy:

- Limbs: Short & deformed.
- Trunk: Short & deformed.

3. Osteogenesis imperfecta:

- BONES: Fragile bones → multiple fractures → malunion → dwarfism.
- EYES: Blue sclera.
- EARS: Conductive deafness.

4. Rickets.

5. Pott's disease of the spine.

D) Genetic diseases

1. Laurant Moon Biedle syndrome.

2. Mongolism.

3. Turner's syndrome: primary amenorrhea, sexual infantilism, short stature.

4. Progeria: premature senility.

E) Familial & racial.

1. Breath: Rapid deep breathing (Kussmaul's)
2. Brain: Confusion, then Coma.

TREATMENT

- IV sodium bicarbonate.

Hyperparathyroidism is not the only cause of HCA

* functions of Ca:

1. Ms contraction (actin over myosin)
2. Neuromuscular transmission
3. Bone & teeth
4. Coagulation system

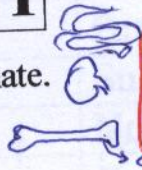
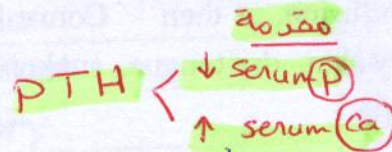
* Normal Levels

total Ca : 8.5 - 10.5 mg/dl
P : 2.5 - 4.5 mg/dl

- * ↑ Ca & ↑ P = Acromegaly
- * ↓ Ca & ↓ P = malabsorption

نمیتواند که الحاحات را برطرف کند
ده تزوید و العکس

albumin ↓
nephrotic syndrome
serum Ca normal
also Albumin must be normal



1. intestine: ↑ absorption (act. vit D)
2. Kidney: ↑ reabsorption, & ↑ excretion of P
3. Bone: ↑ resorption (↑ osteoclastic activity)

control # vit D
so, ↓ serum Ca

if pH normal → 50% ionized
50% non "

if pH ↑ (alkalosis) → ionized ↓

if pH ↓ (acidosis) → ionized ↑

pH
مالتواند
total Ca
(لا تغییر)

shift به
ionized
& non "

ionized 50%

nonionized 50%

40%

Pln Bound
(on Albumin)

10%

inorganic

Ca phosphate

Ca citrate

IBD, OM, parathyroid
→ Kid & Gall stones

مقدار کل کلسیم
Total Ca
نه لو. Alb. ناقص

HYPERPARATHYROIDISM

ETIOLOGY

1. Primary Hyperparathyroidism

- It is due to parathyroid **adenoma** (single OR multiple).
- Serum Ca & PTH: **increased.** → 1st PTH ↑, 2nd Ca ↑

2. Secondary Hyperparathyroidism

- It is a compensatory **hyperplasia** of the parathyroid due to hypocalcemia.
- It results in increased secretion of PARATHORMONE (PTH).
- It returns to normal after treating the cause of hypocalcemia (e.g. CRF or malabsorption).
- Serum Ca & PTH: **increased. PTH, low or normal Ca.**

3. Tertiary Hyperparathyroidism

- It is an irreversible parathyroid hyperplasia (**Tumour**) after longstanding 2ry hyperparathyroidism.
- Serum Ca & PTH: **increased.**

4. Paramalignant syndrome

- It is associated with increased secretion of PTH from an **ectopic tumour** (e.g. bronchial carcinoma).
- Serum Ca & PTH: **increased.**

CLINICAL PICTURE

I. SKELETAL MANIFESTATIONS

1. Bony pains & backache. (spongy → neck femur spine)
2. Pathological fractures.
3. Osteitis fibrosa cystica: **soft, weak, deformed & replaced by fibrous tissue**

II. EXTRA-SKELETAL MANIFESTATIONS

1. Renal:

- Polyuria: because hypercalcemia will make the renal tubules less sensitive to ADH.
- Renal stones: **multiple, bilateral, recurrent** until correction of hypercalcemia.
- Renal calcification: **nephrocalcinosis** occurs in the renal parenchyma & may end in CRF.

2. CVS:

arrhythmias, hypertension, bradycardia, short QT

3. CNS:

apathy, hypotonia, weakness, (spasm)

4. GIT:

anorexia, nausea, vomiting, constipation, pancreatitis.

5. Skin:

itching.

6. Eye:

conjunctivitis & keratitis.

7. Hypercalcemic crisis:

8. Metastatic calcification in soft tissues,

e.g. arteries.

9. Gallstones

due to ↑ bile flow, Ca deposition in biliary system due to

10. Kidney

accelerates atherosclerosis

11. Premature activation of trypsinogen to trypsin → autodigestion (injury)

① Premature activation of trypsinogen to trypsin → autodigestion (injury)

12. Pancreatic calcification

② Pancreatic calcification

13. White Knight Love

White Knight Love

14. CRF

CRF

15. CRF

CRF

16. CRF

CRF

INVESTIGATIONS

A) CHEMISTRY

1. Blood chemistry:

- Increased Calcium, Decreased Phosphate, Increased Alkaline Phosphatase.

2. Urine analysis:

- Increased Calcium, Increased Phosphate, Increased volume.

not specific
as ↑ in any bone
damage eg: Paget of bone³⁸

↑ bone turnover

increased osteocalcin → >30 King Armstrong
(phosphorus)

1ry, tertiary, PMS

PTH ↑↑↑ Ph. loss

nephrogenic DI

لا تفرز
الكلى
الكلى
kidney to reabsorption

B) HORMONES

3. Hormonal assay:

- Increased level of PARATHORMONE.

4. Steroid suppression test:

- Normally: Corticosteroids lower the serum Calcium by inhibiting vitamin D.
- In disease: Hydrocortisone 40 mg / 8 hours for 10 days will lower the serum Calcium:

i. In Hypercalcemic states. all other causes

ii. Not in Hyperparathyroidism.

as cortisol only inhibits intestine
absorption
bone is not suppressed

C) IMAGING

5. Imaging to localize the parathyroid adenoma:

a) Ultrasonography, CT, MRI.

b) Radio-isotope subtraction scan: digital subtraction imaging

- The neck is imaged during successive injections of 2 radioactive isotopes:

- o Thallium: is taken up BOTH by the thyroid & parathyroid.
- o Technetium: is taken up ONLY by the thyroid.

- Then image subtraction is done by the computer: → a parathyroid image.

6. Imaging for the clinical manifestations:

"X-ray"

a) For the bone:

- Absence of the lamina dura around the teeth.
- Bone cysts. (Howship's Lacunae)
- Cod-fish spine: indentation of the vertebral bodies by intervertebral discs.
- Decalcification: ground glass appearance of the bones.
- Erosion: sub-periosteal erosion of the phalanges.
- Pepper-pot skull: mottling of the skull.
- Densitometry: DEXA, plain xray CT

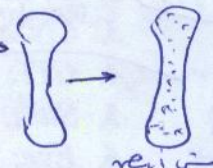
b) For the urinary system:

- Renal stones.
- Renal calcification: nephrocalcinosis.

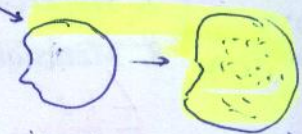
hand layer around sockets



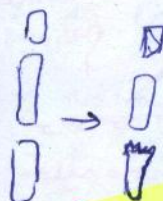
will
disc
appear
as
soft
bone



new
bone



White Knight Love



Spiz
RA.

Localized
opacity

general
diffuse
opacity

Q: Causes of Hypercalcemia

39

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

1. ENDOCRINAL CAUSES

- a) **Hyperparathyroidism:** primary, tertiary, paramalignant syndrome. (all except 2nd)
- b) **Hyperthyroidism:** not suppressed by cortisol
- * c) **Addison's disease:** ↑ intestinal absorption, ↑ bone turn over.
- d) **Acromegaly:** ↓ cortisol → no inhibition of ↑ intestinal absorption

2. IATROGENIC

- a) Hypervitaminosis D.
- b) Calcium.
- c) Diuretics:
- d) Milk-alkali syndrome.

thiazides & furosemide

pt. peptic ulcer & excess ingestion of milk antacid (for H+) → ↑ Ca → constipation, alkalosis

3. MALIGNANCY

- a) Osteolytic metastasis:
- b) PTH secretion:
- c) Prolonged immobilization:
- d) Activation of Vitamin D:

it causes hypercalcemia due to:

& production of osteoclastic factors. in cases of ectopic tumours, e.g. bronchial carcinoma. in terminal cases. (osteoporosis development as in Lymphoma & multiple myeloma)

4. MISCELLANEOUS

- * a) Sarcoidosis. activation of vit D
- * b) Multiple myeloma.
- c) Prolonged immobilization.
- d) Familial hypocalcemic hypercalcemia: a hereditary disease with ↑↑ tubular Ca reabsorption.

↓ Ca - urine
↑↑ Ca - Blood

TREATMENT

I. Surgery:

- Surgical removal of adenomas.
- Surgical removal of most of the hyperplastic tissue in hyperplasia + ttt of the cause.
- Calcium may be needed after surgery. (as osteoblast & RLN injury may occur)

II. Treatment of acute hypercalcemia:

"Hypercalcemic crisis"

- It is an emergency leading to:

- Nausea, vomiting, abdominal pain.
- Polyuria, dehydration, fever.
- Confusion, coma, death.

- It needs immediate ttt which is life saving:

- IV saline: 4 litres / day for 3 days to correct dehydration & wash out Calcium.
- Chelation: IV Biphosphonate (50 mg IV over 5 h), IV Mithramycin (25 mcg IV over 6 h).
- Calcitonin: 200 U / 6 hours IV.
- Prednisolone: 1 mg / Kg / day.
- Hemodialysis: in severe cases.

Metabolic encephalopathy

↓ bone resorption
↑ blast (Bazily)
↓ clast
↑ Ca excretion

1st of all causes of ↑ Ca except Hyperpar

Oral
1st

why? → ↓ Ca serum
How? → by inhibit vit D
when? → in all causes except Hyperpar

- 1 Addison
- 2 Sarcoidosis
- 3 Multiple myeloma

White Knight Love

TETANY

DEFINITION

- Increased excitability of the nerve & muscle.

ETIOLOGY

Parasthesia twitches
spasm
convulsions

I. HYPOCALCEMIA

1. Decreased production of Calcium:

"Hypoparathyroidism"

- Congenital: absence. — rare
- Surgical: removal during thyroidectomy.
- Autoimmune. — rare

2. Decreased intake of Calcium:

- Prolonged starvation, anorexia.

3. Decreased absorption of Calcium:

- Malabsorption syndrome.

4. Increased excretion of Calcium:

- Renal tubular disorders.
- Renal failure.

II. ALKALOSIS

- Total Calcium is kept constant BUT ionized fraction is decreased leading to Tetany.

1. Metabolic alkalosis.
2. Respiratory alkalosis.

Refer to "Nephrology"

استرجع كتابه

III. HYPOMAGNESEMIA

"Rare"

- Magnesium deficiency causes increased neuromuscular excitability → Tetany.

1. Malabsorption syndrome.
2. Diuretics: thiazides & furosemide.
3. CRF. ↓ reabsorption of Mg
4. Diminished intake: e.g. malnutrition.

CLINICAL PICTURE

I. LATENT TETANY

- Manifestations of tetany are not present.
- Manifestations appear by PROVOCATIVE TESTS.

1. Chvostek test:

- Tapping of the facial nerve in front of the ear → contraction of the facial muscles.

2. Trousseau's sign:

- Inflating the sphygmomanometer above SBP for 3 minutes → carpal spasm.

3. Erb's sign:

- Stimulation of nerves by less than 4 milli-amperes → muscle contraction, (normally: 8 milli-amperes at least are needed for stimulation).

II. MANIFEST TETANY

- Manifestations of tetany are present.

1. Irritability & parasthesia.

2. Muscle twitches & may be convulsions in severe cases.

3. Carpo-pedal spasm: spasmodic attacks affecting the carpal & pedal muscles.

4. Spasm of other muscles:

- | | | |
|-----------------------------|---|----------------------------------|
| • Eye lids | → | Blepharospasm. |
| • Laryngeal muscles | → | laryngismus stridulus. (stridor) |
| • Facial & masseter muscles | → | risus sardonicus & trismus. |
| • Diaphragm | → | hiccough. |
| • GIT | → | abdominal colics. |

5. Ectodermal changes: (Only in Hypocalcemia)

- Skin: atrophic, rough, falling of hair.
- Nails: brittle.
- Teeth: hypoplastic. loosening (also DM)
- Eye: cataract.

INVESTIGATIONS

1. In Hypoparathyroidism:

- Decreased serum Calcium, Decreased serum PTH, Increased serum Phosphate.

2. In Alkalosis:

- Normal serum Calcium, Normal serum PTH, Normal serum Phosphate.
- Decreased serum ionized Calcium.
- Increased pH.

3. In Hypomagnesaemia:

- Decreased serum Magnesium.

V. slowly
A. myophyl.
B. stimulant
Ca
Digitalis

TREATMENT

A) Treatment of the attack:

oral

also in the

- anaphylaxis
- tetany
- Hyperkalemia

to antagonize effect of K on Heart

- IV Ca gluconate: 10 ml of 10% solution over 10 minutes (very slowly) IV).

Cardiac arrest at systole

B) Treatment in between the attacks:

1. In Hypocalcemia:

- Ca gluconate: 1 - 3 mg / day orally.
- Vitamin D (cholecalciferol): 50,000 U / day orally.
- A T 10 (Dihydroxycholesterol): 0.5 mg / day orally.
- It increases Ca absorption from the intestine & phosphate excretion in urine.

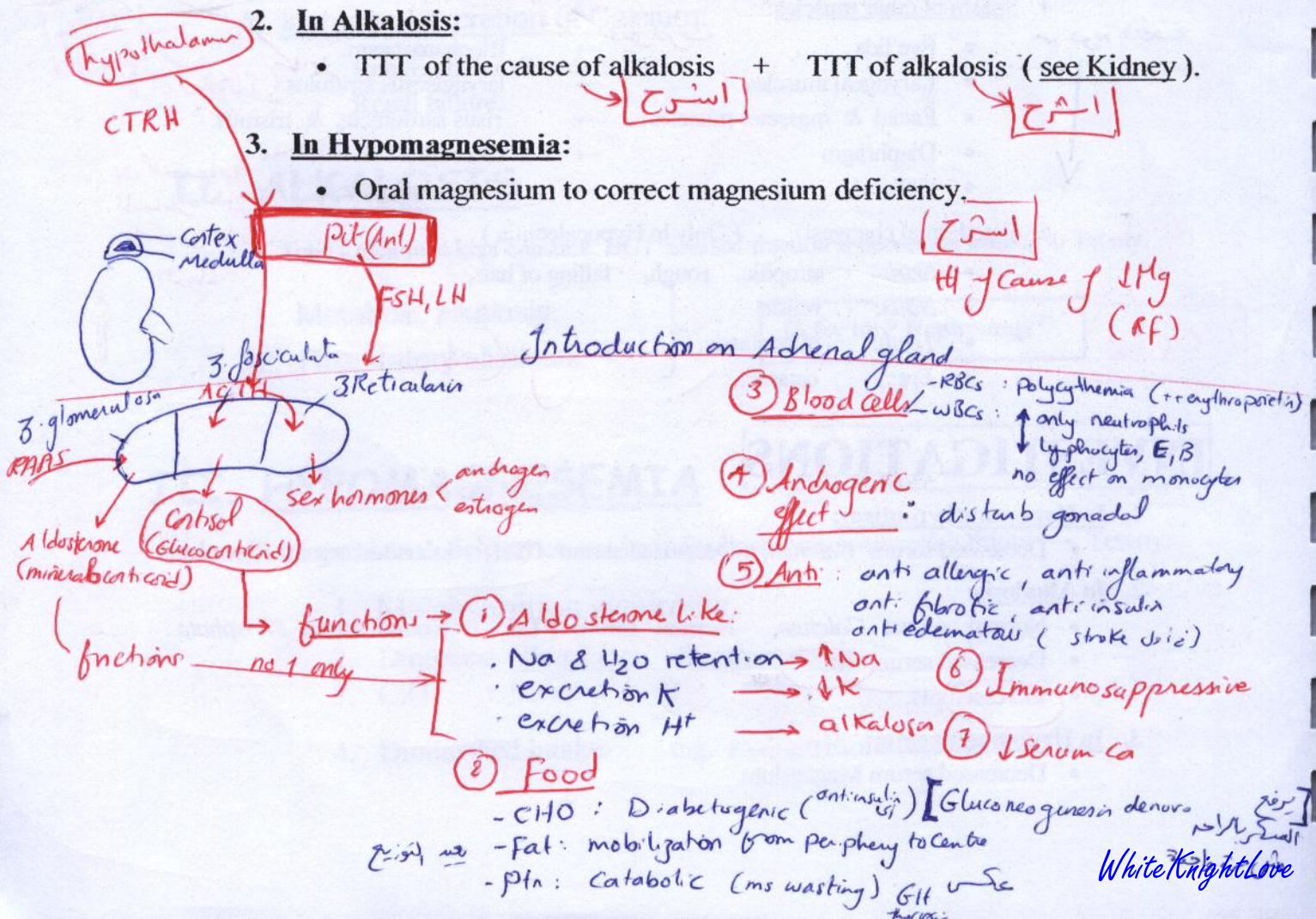
antitetic

2. In Alkalosis:

- TTT of the cause of alkalosis + TTT of alkalosis (see Kidney).

3. In Hypomagnesemia:

- Oral magnesium to correct magnesium deficiency.



CUSHING'S SYNDROME

Q Diagnostic evaluation

DEFINITION

- It is a clinical state resulting from: INCREASED GLUCOCORTICOIDS.

ETIOLOGY

A. IATROGENIC

لا يتم
مستور
وسين
منه انما

1. Prolonged administration of corticosteroids (Cushingoid syndrome):
2. Prolonged administration of ACTH (Cushingoid syndrome):

ما يكون سبب دوامه برا يعني اسه
Cushingoid

"The most common cause"

Exogenous cortisol
adrenalin rule of
B.A.

common.
less common - as multiple sclerosis

B. SPONTANEOUS

"The rare cause"

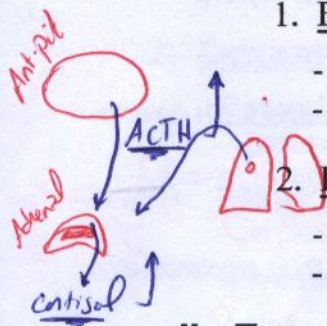
endogenous cortisol
مرحله بنج كورتيزول

I. Excess ACTH secretion:

1. Excess Pituitary ACTH secretion: = CUSHING'S DISEASE

not syndrome

- It occurs in pituitary tumours (pituitary adenoma).
- It represents 70 % of the spontaneous type.



2. Ectopic ACTH secretion:

- It occurs in paramalignant syndrome (e.g. bronchial carcinoma).
- It represents 15 % of the spontaneous type.

في ال حالات
cortisol ↑
(Cushing)

II. Excess cortisol secretion:

- It occurs in primary adrenal tumours (e.g. adenoma or adenocarcinoma).
- It represents 15 % of the spontaneous type.

1- في
adrenal tumor
ACTH ↓
by negative feed back

CLINICAL PICTURE

case clinical

- INCIDENCE: Age: 20-40 years, Sex: more common in females.

1. Disturbances in Fat metabolism:



- Moon-face: rounded face with bloated cheeks.
- Trunkal obesity: central obesity:
 - Increased fat in breasts & abdominal wall.
 - Hollow buttocks & thin limbs.
- Buffalo-hump: increased fat in the interscapular region.

fat →

Pit tumor & Lo! .
high ACTH
PMS & Lo! .
V.V. high ACTH
لانه في حاله
تفرز كثر ادى

2- في
E ACTH ↑
also MSH ↑ (pigment)
in pit tumor only
الوجه الداكن
hyper pigmentation

Lo! PMS
ACTH ↑
طاح

Oral
hyperpigmentation في Cushing
Pit. tumor
White Knight Love

fatal mistake - case curly :
in case Addison :
curly → polyuria
Addison → polyuria } different mechanisms

أولى تقول أبدأ في
anemic ← هشاشة
تبقى في الدم حاجة

حوار شفوي
أسباب
ery (drugs)

44

2. Disturbances in Protein metabolism:

- Muscles: wasting, weakness, myopathy.
- Bones: osteoporosis → backpain, kyphosis, pathological fractures.

Skin:

① Thin skin.

② Poor healing of wounds.

③ Vascular purpura:

④ Red striae (striae rubra):

⑤ Stria alba: stretch

not calcium affection
but more: ptn affection

due to ↓ collagen in B.V. wall (Catabolic on ptn)

Bruising due to ↓ support of the blood vessels. (↓ collagen) fragile

purplish lines on the trunk & thighs due to:
rupture of the weak SC collagen fibres → exposure of the vascular SC tissue.

⑥ ↑ skin infections (↓ immunity)
Bact. fungal

3. Disturbances in Carbohydrate metabolism:

- Hyperglycemia & may be Secondary Diabetes (Steroid Diabetes).

4. Disturbances in Fluid & Electrolytes:

- Sodium: retention leading to hypertension.
- Potassium: loss leading to hypokalemia & polyuria (K diuresis).
- Alkalosis & tetany.

5. Other manifestations:

- Psychological symptoms: usually depression.
- Polycythemia: plethoric face. (+ + erythropoietin)
- Pigmentation of the skin: only in cases of excess ACTH secretion, as MSH is part of ACTH molecule.
- Infections: especially skin infections (fungal & bacterial). (imm ↓)
- Impaired growth: growth retardation occurs in children. catabolic effect against anabolism of G-H
- Impaired gonadal function: female: amenorrhea, hirsutism, acne, male: ↓ libido, impotence, acne.

INVESTIGATIONS

I. Investigations to diagnose Cushing's syndrome:

1. Cortisol level in plasma:

- Normally: 5-20 ug % & there is normal circadian rhythm (lowest at midnight)
- In Cushing's: early: loss of circadian rhythm, late: persistent cortisol elevation.

2. Corticosteroid level in urine:

- Elevated urinary corticosteroids.

3. Blood chemistry:

- Increased Glucose, Increased Na, Decreased K.

4. Blood picture:

- RBCs: increased.
- WBCs: increased neutrophils, decreased lymphocytes, eosinophils, basophils.

فحص

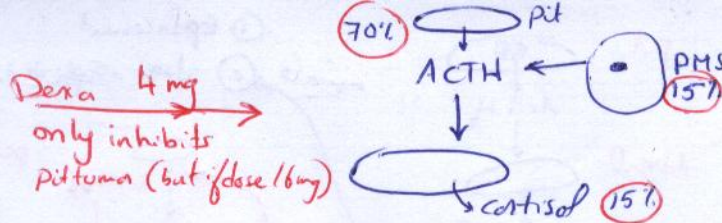
Oral
هو لار
أول
لأنه في
early loss of rhythm
میں

plasma level
8 urine
not suppressed by low Dexa

(highest at 8 am) 20
(lowest at midnight) 5
>20
عند حول
المعروف

أول مؤشر
هو تلك ثلاثي بالليل بدل
سبق 15 أو 20

Cortisol → ↓ Ca (by ↓ vit D)
→ ↑ Ca (by bone resorption) → فظيل Ca هو قو



عمره ما يقلل
يجعل على
عمره ما يقلل
يقلل بياض
45

5. Dexamethazone suppression test "low dose":

from Conn's disease of diagnosis

• Method:

- Dexamethazone (synthetic glucocorticoid) is given in a **low dose**: 0.5 mg / 6 h for 2 days.

4 mg in total
في اليومين

• Result:

- Normally:

cortisol level in the blood is suppressed, because:
Dexamethazone will inhibit ACTH by -ve feedback.

- In Cushing's syndrome:

cortisol level in the blood is not suppressed, because:
there is pathological secretion of either ACTH or cortisol.

لو ما قللت
cortisol

بقدر مرضه انه
مضطرب

بس ما مرضت اذن نوع

لوقال الكورتيزول يبقى
exclude Cushing

6. Insulin-induced hypoglycemia:

- Normally:

it stimulates increase in plasma cortisol.

- In Cushing's syndrome:

no increase in plasma cortisol.

II. Investigations to diagnose the cause:

1. Plasma ACTH:

- **Low:** in primary adrenal tumours (due to inhibition of ACTH by -ve feedback).
- **High:** in pituitary tumours secreting excess ACTH.
- **Very high:** in ectopic tumours (as bronchial carcinoma) secreting much excess ACTH.

2. Dexamethazone suppression test "high dose":

• Method:

- Dexamethazone (synthetic glucocorticoid) is given in a **high dose**: 2 mg / 6 h for 2 days.

• Result:

- In pituitary tumour:

cortisol level in the blood is suppressed.

- In adrenal & ectopic tumours:

cortisol level in the blood is not suppressed.

لا
ما على

+

التفرقة clinically

بال pigmentary

3. Imaging:

a) Abdominal CT, MRI, or ultrasonography:

- To detect adrenal tumours.

b) Skull CT, MRI:

- To detect pituitary tumours.

c) Chest X-ray & CT:

- To detect bronchial carcinoma.

الحياة! الى عند
suppressed الذي يبقى
by high dose Dexa
pit tumor هو

DIFFERENTIAL DIAGNOSIS

1. From other causes of obesity.
2. From other causes of hirsutism.
3. From other causes of hypertension. eg Hyperpara
4. From other causes of diabetes. eg Hemochromatosis
5. DD of the cause.
6. other causes of Polyuria eg: DM, DI, Hyperpara

TREATMENT

1. For adrenal tumours:

- Surgical removal of the tumour followed by suboptimal replacement therapy (low dose corticosteroids) for several months till the other atrophic gland recovers from suppression.

2. For pituitary tumours:

“ Cushing's disease ”

- Surgical removal or irradiation of the tumour, followed by replacement therapy.
- Nelson's syndrome: ttt of pituitary Cushing's disease by bilateral adrenalectomy may lead to the development of a locally invasive pituitary tumour with very high levels of ACTH & Hyperpigmentation.

3. For bronchial tumours:

“ Paramalignant syndrome ”

- TTT of the primary tumour, if possible.

surgery or chemotherapy

ADDISON'S DISEASE (CHRONIC ADRENAL FAILURE)

ETIOLOGY

I. PRIMARY ADRENAL FAILURE (Addison's disease)

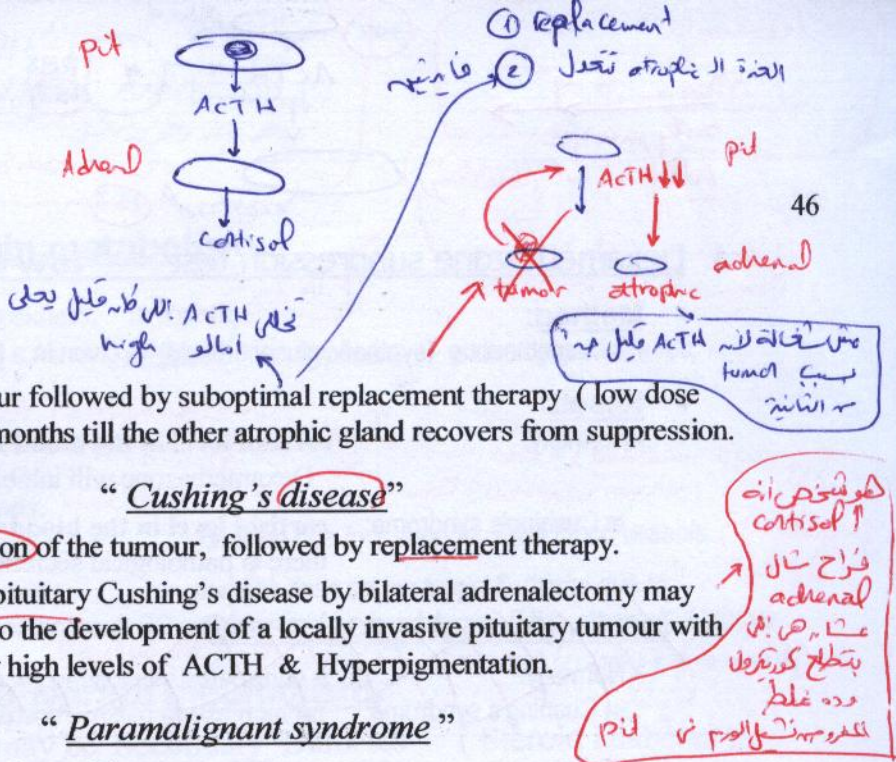
- Due to primary failure of the adrenal glands:

- **I**mmune: Autoimmune disease is the most common cause (80 %).
- **I**nfection: TB, HIV, Fungal.
- **B**ilateral: adrenalectomy.
- **B**ilateral: adrenal hemorrhage or infarction.
- **M**alignancy: Metastases especially from bronchial carcinoma, Lymphoma.
- **M**etabolic: Amyloidosis, Hemochromatosis.
- **C**ongenital: Hypoplasia & Hyporesponsiveness to ACTH.

II. SECONDARY ADRENAL FAILURE

- Due to secondary failure of the adrenal glands:

- Hypothalamic or pituitary disease, causing decreased ACTH level.



scheme for Cushing

المنهج
الكليني

CIP:

trunkal Obesity (fat), Osteoporosis (ptn), DM^{2ry} (CHO), HTN^{2ry} (electrolyte), Hirsutism, amenorrhea (others)



Investigating: cortisol (plasma, urine), DST (low dose)

do DST (high dose)

suppressible

not suppressible

70%

Pit Cushing (Cushing disease)

CIP: hyperpigmentation

Confirm

- lab: ↑ACTH
- Imaging: Brain CT & MRI

15%

Adrenal

low

confirm

Imaging: abdomen

15%

Ectopic (PMS)

ACTH ↑↑↑ high

Confirm

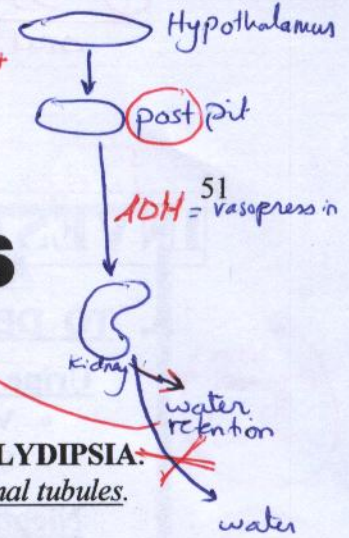
Imaging: chest

H/O Jatrogenic Cushing

White Knight Love

لا يفرغ الكلى زائداً على حاجته
stimulation
Hypothalamus
B.v. ينقل
فيحافظ على الضغط العالي
hypertension
يصاحبه الـ

hypothalamus تنبأ بـ B.v.
Osmoreceptors
osmotic pr. $\uparrow\uparrow$
(Na $\uparrow$)



DIABETES INSIPIDUS

DEFINITION

- It is a clinical state of: **POLYURIA**, **NOCTURIA** & compensatory **POLYDIPSIA**.
- It is due to: deficiency of ADH, or lack of response to its action by the renal tubules.

ETIOLOGY

I. PITUITARY "CRANIAL" DI

"Deficiency of ADH"

- There is deficiency of ADH due to: damage of hypothalamus, posterior pituitary or hypothalamohypophyseal tract:

- **Idiopathic:** The most common cause.
- **Intracranial tumours:** primary or secondary or pituitary tumours.
- **Infections:** TB, meningitis.
- **Infiltrations:** Sarcoidosis.
- **Injury:** Head surgery (to the pituitary), Head trauma.
- **Irradiation:** Post-radiotherapy (to the pituitary).

1. BV osmoReceptor
2. Hypothalamus & post pit
3. Kidney

II. NEPHROGENIC DI

"Defect in the renal tubules"

- There is lack of response of the renal tubules to the action of ADH:

- Hereditary.
- Acquired: hypercalcemia, hypokalemia, drugs as Lithium.

III. FAMILIAL DI

"Defect in the osmoreceptors"

- There is a hereditary defect in the osmoreceptors making them insensitive to changes in the osmotic pressure of plasma.
- This type is also called: essential hypernatremia.

CLINICAL PICTURE

1. Polyuria: marked **polyuria** by day & night (3-15 litres/day) & compensatory **polydipsia**.
2. Dehydration: & may be hypovolemic shock & may be ARF.
3. Complications of hypernatremia: hypertonic encephalopathy* (lethargy & coma).
4. Features of the cause: e.g. pressure manifestations of a tumour.

Na $\uparrow$ in ECF $\rightarrow$ water gets out of cells
Brain cells shrinkage

White Knight Love

الإنسولين، الجلوكوز، $\text{ADH} \uparrow$ ، والدورة تغفل

Low fired sp gl. $\rightarrow$ also in R.F.
بفیرآخ

N: 1015 - 1025

- Volume: 3 – 15 litres / day.
- Specific gravity: Low (1001 – 1004) & fails to increase with fluid restriction.

- Give nicotine (1–3 mg by injection): → stimulation of the hypothalamus & oliguria.
- The response is negative in: pituitary DI.

- Low level.

- X-ray, CT, MRI to detect tumours.

“ Give IV Vasopressin ”

- Oliguria occurs in: *normal persons, pituitary DI, familial DI.*
- The response is negative in: *Nephrogenic DI* → *ADH*

- Give NaCl 2.5 cc of 2.5 % solution per Kg: → stimulation of the osmoreceptors & oliguria.
- The response is negative in: Familial DI.

- *In DI:* urine volume remains big & specific gravity remains low.
- *In hysterical polydipsia:* urine volume decreases & specific gravity increases.

(desmopressin) سجائی

- (in cases of NDI)

- They probably work by sensitizing the renal tubules to endogenous vasopressin.

in liberal amounts.

if possible. eg: removal of pit tumor

DIFFERENTIAL DIAGNOSIS OF POLYURIA

* Polyuria = ↑ urine vol. > normal (N: 1-1.5 L)

I. Renal causes:

- Chronic renal failure.
- Polyuric phase of acute renal failure.
- Nephrogenic DI.
- Renal tubular disease.

most common renal cause

II. Endocrinal causes:

- Diabetes insipidus.
- Diabetes mellitus.
- Hyperparathyroidism & Hypercalcemia.
- Cushing's syndrome, Addison's disease & Conn's syndrome.

osmotic diuresis

most common endocrinal cause

III. Functional causes:

- Exposure to cold weather.
- Excessive intake of: fluids, coffee, tea.

IV. Hysterical polydipsia:

- Water deprivation test.

Q: Causes of polyuria: as cause of ARF

HIRSUTISM

DEFINITION

- Excessive growth of body hair in females.

ETIOLOGY

A. HIRSUTISM WITHOUT VIRILIZATION:

1. Idiopathic: the most common cause.
2. Iatrogenic: minoxidil, androgens, cyclosporin.
3. Familial & Racial.
4. Polycystic ovary: mild cases.

B. HIRSUTISM WITH VIRILIZATION:

1. Congenital adrenal hyperplasia.
2. Adrenal tumours.
3. Ovarian tumours.
4. Polycystic ovary: severe cases.

أمة ليس يهملها الله فهو معقود على كل الحاشي
بيت يموت الفار خلف جداره جوماً وبيت بالموائد مخف
تأكل لذل وتستفسر، لظماً وتنادي لا أريد إلا السلامة
فما نفعت أحاً وما دفعت غنياً وما رفعت راح

54

GYNECOMASTIA

حفظ
للاضوي
8 clinical

DEFINITION

- Enlargement of the male breast due to hypertrophy of the glandular tissue.

ETIOLOGY

"Decreased androgen / estrogen ratio"

1. Physiological:

- Neonatal ($\uparrow$ estrogen), pubertal ($\uparrow$ estrogen), old age ($\downarrow$ androgen).

2. Pathological:

a) Endocrinal: Hypogonadism, Hypothyroidism, Hypothyroidism.
b) Metabolic: Chronic renal failure, Liver cell failure.
c) Malignant: Estrogen-producing tumours of the testis or adrenals.

failure.
spironolactone (ascites)
Cimetidine (gastitis)

3. Iatrogenic:

- Estrogen,

Digitalis,

Spironolactone,

Cimetidine.

H₂ receptor blockers

4. Idiopathic.

HYPOGLYCEMIA

ETIOLOGY

1. Endocrinal:

- Hypopituitarism. Simmond's, Sheehan
- Addison's disease.
- Hyperinsulinemia: overdose of insulin, insulinoma, paramalignant, CRF.
- Myxedema Coma

2. Non - Endocrinal:

- Decreased glucose intake: starvation.
- Decreased glucose absorption: malabsorption.
- Increased demand: heavy exercise & pregnancy.
- Increased loss: renal glycosuria.
- ACUTE LIVER FAILURE.

CLINICAL PICTURE

1. Insufficient glucose to the brain leading to:

- Lack of concentration, mental dullness, hallucinations, tremors, convulsions, coma.

2. Manifestations of sympathetic overactivity due to hyperadrenalism:

- Irritability, tremors, pallor, sweating, palpitation (tachycardia).

VC

INVESTIGATIONS

1. Blood: markedly low blood glucose (less than 50 mg / dL).
2. Urine: no glucose in urine.

3. Investigations for the cause.

eg. insulinoma

except renal glycosuria

DKA: glucose = urine

N: 70 - 110 mg/dl
fasting
لا نريد
110

TREATMENT

1. TTT of the cause.
2. TTT of hypoglycemic coma: "refer to DM".

eg: insulinoma: surgical removal

شرح

OBESITY

SQ: complications of obesity
[oral]

DEFINITION

- A state of excess ADIPOSE tissue mass.

ETIOLOGY

I. IDIOPATHIC (95 %)

1. Familial: genetically determined factors or same pattern of eating.
2. Excessive caloric intake: excessive intake of fats or carbohydrates.
3. Diminished caloric consumption: physical inactivity.

عادات تأكل كثير

ناكل أكثر من حاجته فيتم
adipose

II. SECONDARY

1. Endocrinal: Cushing's syndrome, Myxoedema, Hypogonadism, Insulinoma, Pregnancy.
2. Hypothalamic disturbances: Diabetes insipidus, polyphagia, obesity, hypersomnia.
3. Drugs: they stimulate the appetite, e.g. insulin, CCPs, corticosteroids.

↑ lipogenesis
↓ lipolysis
stimulate appetite

MEASUREMENT

1. **Body Mass Index (BMI)** = $\text{Weight} / \text{Height}^2$ (Average: 18 - 25).
Mild (BMI = 27 - 30), Moderate (BMI = 30 - 40), Marked (BMI > 40).
2. **Anthropometry:** measure the skin fold thickness, e.g. over the Triceps.

25 - 27
over wt
سليم
Sunderent

DISTRIBUTION OF BODY FAT

- Measure the: WAIST / HIP ratio:

1. Male (Android) pattern:

- More fat in the upper body (associated with more morbidity & mortality).

Abdominal
Apple



2. Female (gynecoid) pattern:

- More fat in the lower body (associated with less morbidity & mortality).

pelvic
pear



COMPLICATIONS

1. METABOLIC SYNDROME:

- Refer to "DM".

syndrome X

2. CARDIOVASCULAR:

- Coronary artery disease.
- Hypertension.
- Hyperlipidemia & Atherosclerosis.
- DVT & Varicose veins.

(risk factors of obesity
on coronary)

- 1- physical inactivity (for collateral)
- 2- Diet rich in saturated fat
- 3- Hyperlipidemia

3. RESPIRATORY:

- Restrictive hypoventilation & Pickwickian syndrome.
- Sleep apnea syndrome. & intermittent cessation of breathing during sleep

1
2
3
4

marked obesity > 40 kg/m²
Secondary Polycythemia (severe hypoxia)
Hypocapnic hypoxemia
Bony from somnolence (Cushing's)

4. GIT:

- Cholesterol gall stones & cholecystitis.
- GORD & Hiatus hernia.
- Fatty liver.

5. NEUROLOGICAL:

- Cerebrovascular Stroke.
- Carpal tunnel syndrome. entrapment

6. JOINTS:

- Osteoarthritis. esp. knee → hip → lower spine
- Back pain.
- Increased incidence of gout.

7. MALIGNANCY:

- Increased incidence of: cancer colon, rectum, GB, breast.

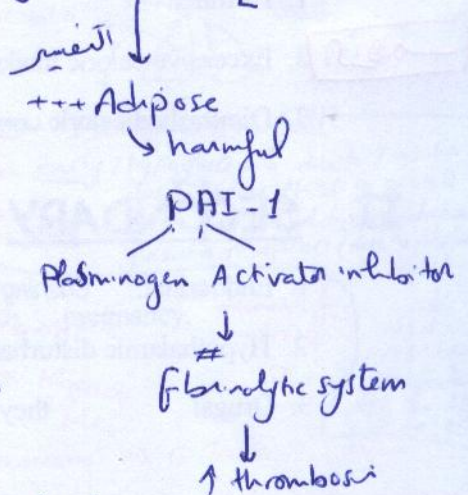
8. PSYCHOLOGICAL:

- Depression, Anxiety.

4. DM (II)

5. High risk for Coagulation

Coronary
Stroke



as fat
→ Restrictive
hypoventilation

Weakness
apnea

+ CO₂, O₂ ↓, pH ↓

potent
stimulus
for RC
(intermittent)

degenerated cartilage by wt
esp. knee → hip → lower spine

↑ intake of pth
Insulin resistance → ↑ U.A.
risk

TREATMENT

1. Reduction in caloric intake:

"Diet ttt"

- The aim is to lose 1 kg / week.

2. Increase in caloric loss:

"Exercise"

- It should be encouraged, BUT: *exercise alone is not enough to lose weight.*

3. Drugs:

a) Anorexic drugs:

e.g. fenfluramine.

b) Oleristat:

inhibits the pancreatic lipase & so decrease fat absorption.

~ Diet

↓ appetite

or (Biguanides) for diabetic

malabsorption

4. Surgery:

a) Jejunio-ileal bypass:

causes malabsorption (not used now) X

b) Gastric balloon:

a balloon is placed endoscopically in the stomach & inflated.

c) Gastric plication:

stapling across the stomach will produce a small gastric pouch.

OSTEOPOROSIS

DEFINITION

Reduction in the BONE MASS leading to:

- Increased bone fragility.
- Increased risk of fracture. *esp trabecular spine neck femur*

ETIOLOGY

1. POST-MENOPAUSAL (Type I). → $\downarrow$ Estrogen } needed for good osteoblastic activity
2. OLD AGE *men* (Type II). → $\downarrow$ Androgen }
3. Endocrinal: *Ca* Cushing's syndrome, Hypogonadism, Hyperthyroidism, Hyperparathyroidism. *Pln*
4. Failure: Renal failure, Liver failure, failure of absorption (MALABSORPTION). *turn over $\downarrow$ $\uparrow$ Ca - Blood*
5. Malignancy: Multiple myeloma, terminal malignancy, osteolytic metastasis. *vit D*
6. Iatrogenic: Corticosteroids, long term heparin, long term diuretics.
7. Inherited: Osteogenesis imperfecta.
8. Immobilization. *bone wasting*
9. Idiopathic.

CLINICAL PICTURE

1. EARLY:

- Asymptomatic.

2. LATE:

- Bone pains & Bone tenderness.
- Pathological fractures & Deformities.

esp spine: Kyphosis

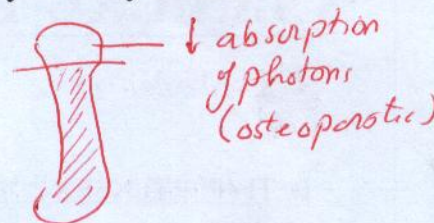
INVESTIGATIONS

1. Plain X-ray:

- Decreased bone density (osteopenia).
- Deformities, fractures, vertebral collapse.

2. Bone Densimetry:

- Measure the bone mass by: Dual Energy X-ray Absorptiometry "DEXA".
- It measures: the absorpti on of a beam of photons generated by an X-ray source to determine the BONE DENSITY.



TREATMENT

1. GENERAL MEASURES:

- Diet: adequate Proteins, Calcium, Vitamin D.
- Calcium carbonate orally.
- Vitamin D orally.

2. HORMONE REPLACEMENT THERAPY (HRT):

- Estrogen therapy: especially in premature menopause, ovariectomy, hypogonadism.
- Androgen therapy: should be given to hypogonadal men.

3. BIPHOSPHONATES:

- They inhibit bone resorption.

also chelate
- ↑ Ca = blood

4. CALCITONIN.

- inhibit bone resorption

Nasal spray

(Miacalcin)

5. TTT of the cause:

e.g. Cushing's syndrome.

PHEOCHROMOCYTOMA سيفو

DEFINITION

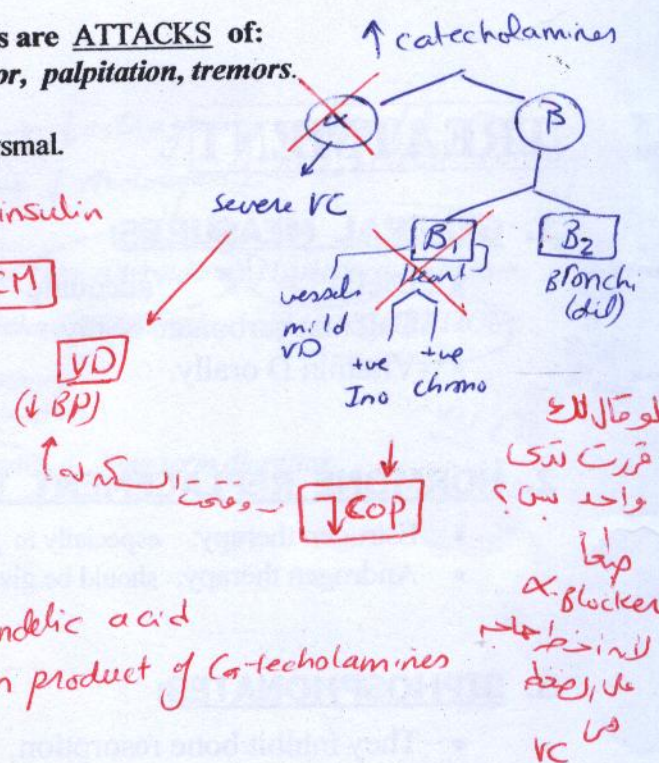
- Tumours that secrete CATECHOLAMINES.
- 90 % arise in the ADRENAL MEDULLA, others in the sympathetic chain in abdomen.
- 90 % are UNILATERAL.
- 90 % are BENIGN.

Adrenaline, Nor Adrenaline, $\pm$ dopamine
(pulsatile in paroxysms)

CLINICAL PICTURE

1. GENERAL: the commonest symptoms are ATTACKS of: headache, sweating, pallor, palpitation, tremors.
2. HYPERTENSION: secondary & paroxysmal.
3. DIABETES: secondary. as anti insulin
4. HYPERTROPHIC CARDIOMYOPATHY. HCM

Oral



INVESTIGATIONS

1. INCREASED CATECHOLAMINES:
- In plasma & in urine.
2. INCREASED URINARY VMA.
3. IMAGING:

- CT, MRI: of the abdomen.

- **MIBG**: scanning with **M**eta **I**odo **B**enzyl **G**uanidine produces specific uptake in sites of sympathetic activity.

detect overactivity
Localize site of overactivity

TREATMENT

1. Surgical: removal of the tumour is the ttt of choice if possible.
2. Medical: combined alpha & Beta adrenergic blockers:
 - For pre- & post- operative ttt.
 - If surgery is not possible.

introduction to DM

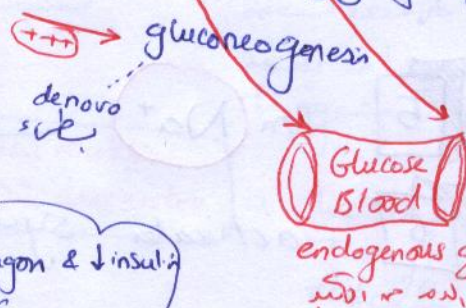
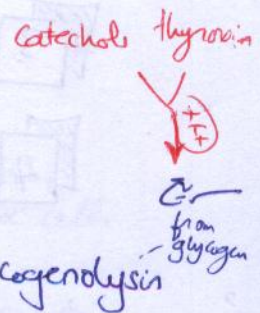
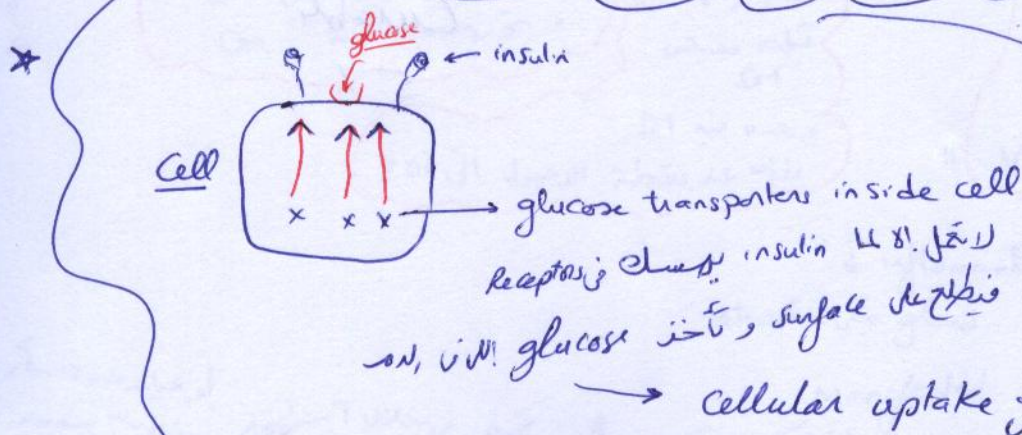
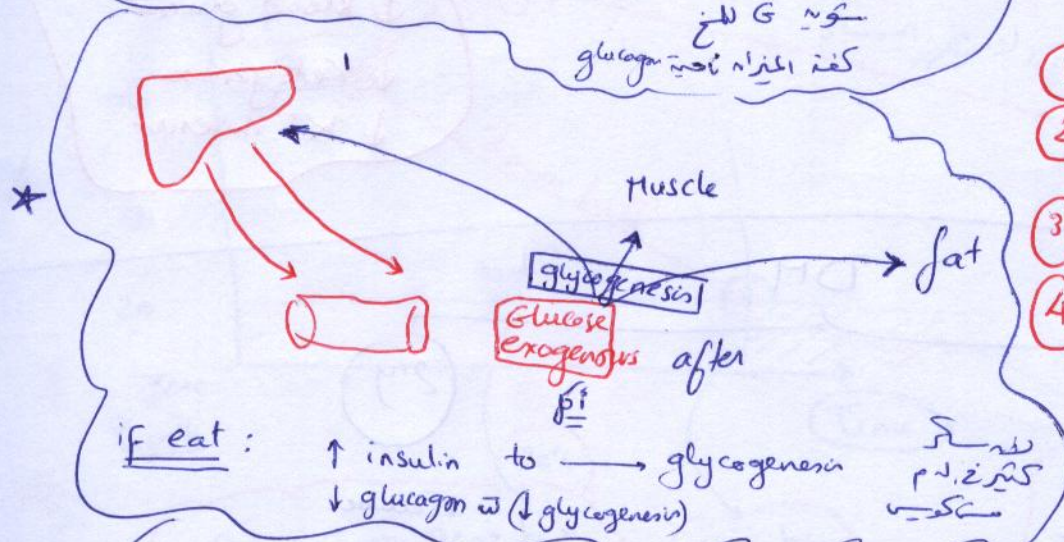
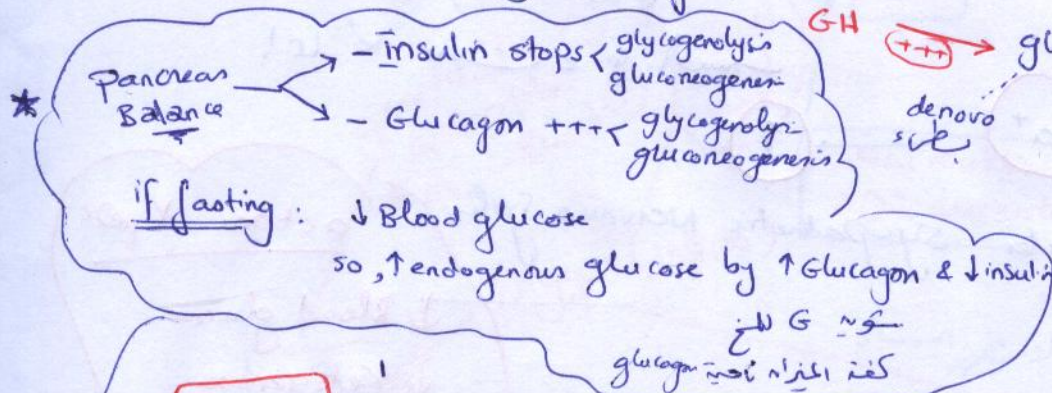
hormones

↓ glucose
insulin

↑ glucose
G.H.
Glucagon
Catecholamine
Cortisol
Thyroxine

Insulin

1. polypeptide : multiple a.a.
2. from : pancreas (islet cells $\Rightarrow$ B cells)
3. Receptors : liver, fat, MS
4. Main action : * lowering down of Blood Glucose



- 1 ↓ glycogenolysis
- 2 ↓ gluconeogenesis
- 3 ↑ glycogenesis
- 4 ++ Glucose transporters

فوائد الأنسولين

WhiteKnightLove

1] ↓ Blood glucose

5. other actions

2]

* ↑ Lipogenesis
↓ lipolysis

pt e insulinoma → خفي
pt e IDDM → خالص

* ↓ Ketogenesis

ورده يحتاج
نقطة واحدة
insulin

v. small insulin is
enough to prevent
Keto acidosis

لذلك الحارة الى معسر

insulin
cell

Ketoacidosis هو الـ بيلة

3]

V. mild anabolic (onptn)

4]

on K^+ of body NO Effect

as it shifts it from serum to inside cell
(↓ serum K) *

ك⁺ ثابت في الجسم

5]

on Na^+

→ ↑

6]

activates Sympathetic Nervous system

actions يوتي

↓ Blood glucose

↓ Ketogenesis

↓ K^+ in serum

DM

1y

no Cause
Controllable

95 %

2y

Cause
Curable

5 %

(Cockback 2)
- pericarditis
- pleurisy
- aseptic meningitis
- DM

Complication
GRF
coma emergency
(Clinical) short or long
CRP's
Case
oral 1000

14

DIABETES MELLITUS

DEFINITION

- A chronic disorder characterized by impaired glucose metabolism → **HYPERGLYCEMIA.**
- It is associated with secondary changes in multiple organs → **COMPLICATIONS.**
- It is due to: **Insulin deficiency** (I) **Insulin resistance** (II) OR Both.
- **INCIDENCE:** It is the most common endocrine disease, 1-2% in most of the communities.

ETIOLOGY & PATHOGENESIS

1. PRIMARY DIABETES

TYPE I Insulin Dependent Diabetes Mellitus (IDDM)

- It is also described as:
- It was previously termed:
- It essentially depends on:

"Ketoacidosis prone"
"Juvenile-onset diabetes"
INSULIN in its treatment.

• Predisposing factors:

1. Genetic factors:

- There is association with certain HLA types. - over expressed in this p.t.
- There is 50 % incidence in identical twins.
- There is ↑ risk of inheritance: **30% if both parents are diabetic.**

2. Immunological factors:

- Immunologic markers: Islet Cell Abs (ICAs) & Anti-insulin Abs.
- INSULITIS: Infiltration of pancreatic islets with **LYMPHOCYTES.**
- Associated AI diseases: e.g. **Coeliac dis, Grave's dis, Addison's dis.**

TYPE I DM is further divided into 2 subtypes:

- Type I A: Immune-mediated β cell destruction with **presence** of Immunologic markers.
- Type I B: Idiopathic β cell destruction with **absence** of Immunologic markers.

3. Environmental factors:

- They trigger the autoimmune process: in the genetically susceptible individuals.
- The most important factors are: Viral infection (**Coxsackie & Rubella**).
CMV mumps

• Insulin abnormality:

- **INSULIN DEFICIENCY:** secondary to destruction of the β - cells.

DM most common cause of
P.N
adult blindness
nontraumatic amputations
end stage renal disease
ESRD
- controllable
- no cause
- (> 95 % of DM)

لازم التلاوة مع بصر
genetic & no immun - environm.
also leukemia
مش حيلة
خاطر
also Pernicious anemia
anti parietal cell
& anti intrinsic factor

Hamilton
Oral 1000
>95%
vrr rare <5%
میزة التقي
هو الوقاية
لو طبل زب زب DM
نسبة 30% اقل
دالة screening
لازم موجودة في الدم

لوقتر → IA → اغلوا → immunosuppressant → خلاصة

WhiteKnightLove

Type ①

Genetic

HLA = Human leukocyte Ag
= MHC = Major Histocompatibility Complex

} genes

on chromosome 6

overexpressed

eg: DR₃ DR₄
DQ₂ DQ₈



oral

destruction of B cells

is Selective

B cells only
& sparing α cells

slow

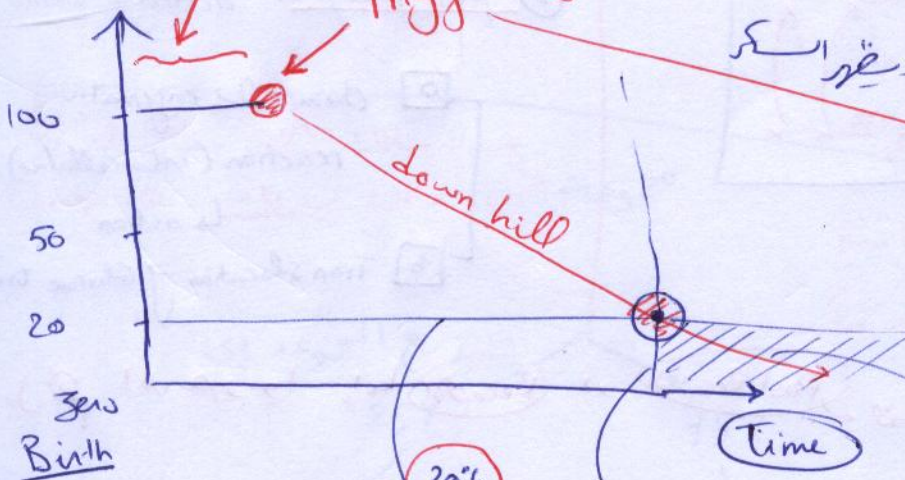
triggering (infection)

when reaches 80% destruction

becomes manifested clinically

قبل که شغل بکند و لا یقرا

لومکاشی حبل
triggering
ده مکاشفی
هیچک



20%
خطر فوته عفیه DM
و حتمه فیه DM

خطر زود
تیه عفیه DM
و بعد فیه DM
لانه عند نقطه الوصول الی 20%

الکیر للباي
20%
بيکونه اسرع
بيکتر خالص
V. Steeping

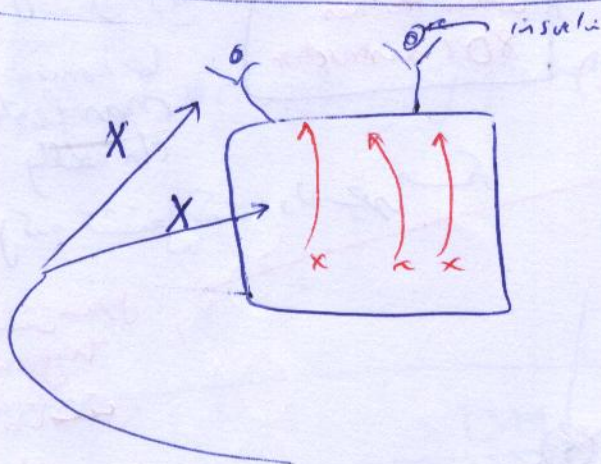
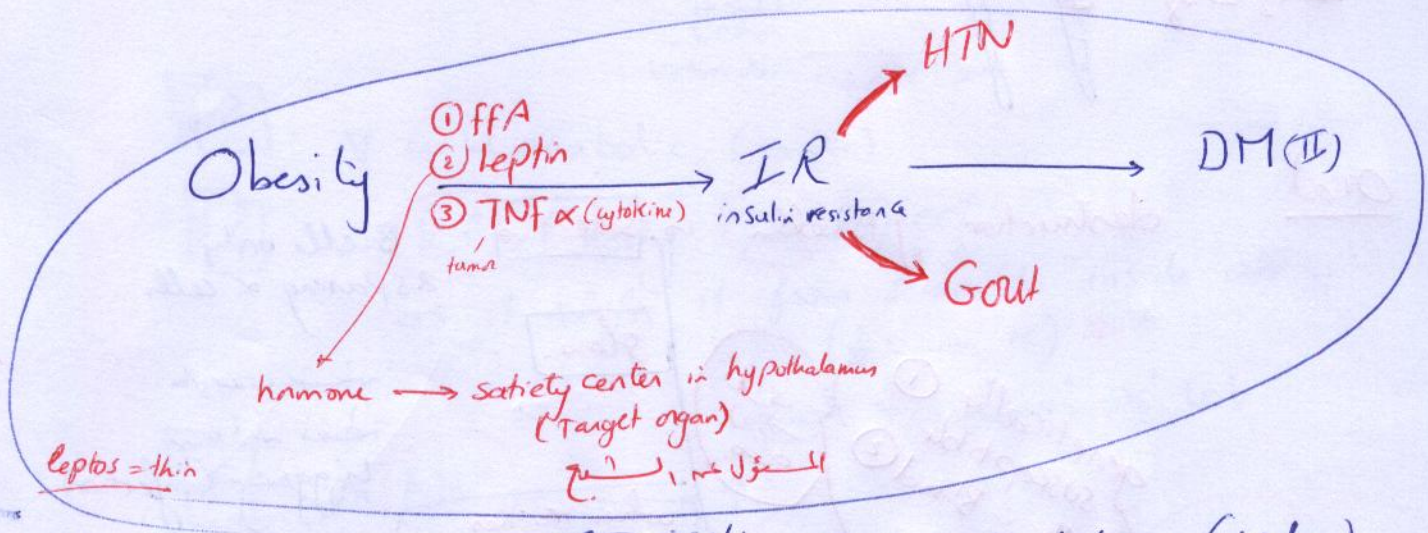
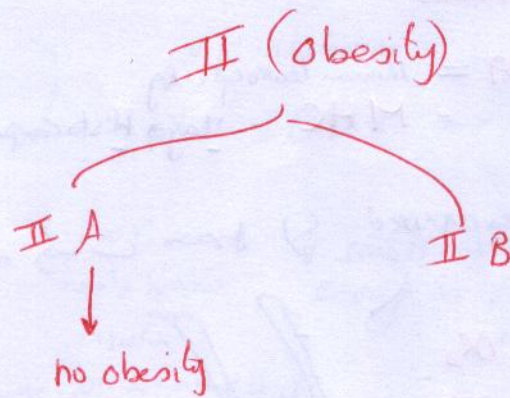
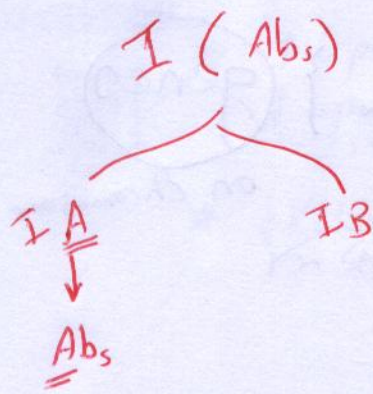
↓ inflammation
atrophic بقی gland

manifested

DM ال

White Knight Love

لومکاشی حبل
بقاوه 3 مینه
من قتلان Ab في دمه
تکفی فر خلا 7 سهر
B cell
لا تکره في کسرت



① Receptor Action (binding)

② post receptor action

- a chemical & enzymatic reaction (intracellular)
 $\rightarrow$ action
- b Translocation of Glucose transporter

٣ دمل ٢م! لا-مخرجا، لا (Receptor) و (Post Receptor) ٢م

لكن هذا الحياه من هيفضل محبى
DKA
لكن متأخر جيتا المرض
يوقى بالانضبط زي
لما في ملاكلا بتوكم

Insulin resistance
وهو عنده
100% ineffective
لكن فيه نوع effect
من كافي انه يمنع سكر
لكن كافرا انه يمنع غيوبة سكر

15

TYPE II Non - Insulin Dependent Diabetes Mellitus (NIDDM)

- It is also described as: "Ketoacidosis resistant".
- It was previously termed: "Maturity-onset diabetes".
- It does not essentially depend on: INSULIN in its treatment.

Predisposing factors:

1. Genetic factors:

- There is no association with certain HLA types.
- There is 100 % incidence in identical twins.
- There is ↑ risk of inheritance: 40 % if both parents are diabetic.

الوراثة هنا أوتوسوم

Risk factors of ID

- Age > 45 y. old
- Family H/O
- Obesity > 27 Kg/m² (JP)
- Gestational DM H/O
- IFG IGT
- HTN (IR) > 140/90

2. Obesity:

- It is absent in: 20 % of the patients
- It is present in: 80 % of the patients
- INSULIN RESISTANCE: due to secretion of

(Type II A).
(Type II B).
Leptin & FFAs.
TNF-α

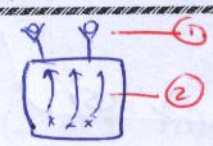
Insulin abnormality:

impaired fasting glucose impaired Glucose tolerance

❖ INSULIN RESISTANCE: "IR"

- Decreased insulin action on target tissues (muscle & liver) due to:

- Receptor defect: ↓ insulin receptors in target tissues (Minor role).
- Postreceptor defect: in target tissues (Major role).



❖ IMPAIRED INSULIN SECRETION:

• Initially:

↑ insulin secretion occurs due to IR to maintain normal glucose

• Later:

↓ insulin secretion occurs due to islet cell failure secondary to "Glucose toxicity".

Persistent
"Hyperinsulinemia".
"Hyperglycemia".

❖ INCREASED HEPATIC GLUCOSE PRODUCTION:

- IR → failure of insulin to suppress gluconeogenesis → Fasting hyperglycemia.

* Sulphonylureas → تحسين السكر ٣ حاجات دول

	Type 1	Type 2
Incidence	10 %	90 %
Age of onset	Less than 30	More than 30
Body weight	Usually decreased	Usually increased
Severity	More severe	Less severe
Complications	More common	Less common
Coma	DKA	Hyperosmolar coma
Insulin level	Low or absent	High (early), low (later)
Insulin therapy	Always essential	Not always essential
Oral hypoglycemic drugs	Not effective	Effective

SPECIAL TYPES

Maturity Onset Diabetes of the Young (**MODY**)

A subtype of type 2 diabetes, but the main defect is impaired insulin secretion & not IR. *not glucose toxicity*

• Etiology:

GENETIC defects in insulin secretion:

(6 variants: MODY 1, **2**, 3, 4, 5, 6 due to mutations in 6 genes).

• Onset:

YOUNG, Early onset of Hyperglycemia:

(Between: 10 – 25 years).

Latent Autoimmune Diabetes of the Adult (**LADA**)

A subtype of type 1 diabetes, but autoimmune β – cell destruction is slow.

• Etiology:

AUTOIMMUNE β – cell destruction.

• Onset:

ADULT, Late onset of Hyperglycemia:

(Above: 30 years).

BRITTLE DIABETES

- A type of diabetes with wide unpredictable fluctuations in blood glucose levels.
- Also called: unstable diabetes or labile diabetes.

قصه عليه وكتب له رسته وظيف له diet راج و جاله رجاهل مضبوط يعني تمام
 له لو جاله من مضبوط اما انه انكه او الدوام مضبوط
 او الكلى له الدوام مضبوط ام فيه مشكلة عنه
 WhiteKnightLove

2. SECONDARY DIABETES

- Cause
- Curable
- (< 5 % of DM)

1. Pancreatic exocrine diseases:

- Chronic pancreatitis, Cancer pancreas, Cystic fibrosis. *malabsorp*
- Hemochromatosis, Pancreatectomy. *in Cancer Insulinoma*

2. Endocrinal diseases: "Increased Anti - insulin hormones"

- Increased GH: *Acromegaly.*
- Increased Glucagon: *Glucagonoma.*
- Increased Catecholamines: *Pheochromocytoma.*
- Increased Cortisol: *Cushing's syndrome.*
- Increased Thyroxin: *Thyrotoxicosis.*

*2ry HTN
Glucagon*

3. Renal diseases:

Chronic renal failure. *late (down regulation of Insulin)*

4. Liver disease:

Chronic liver failure. *IGT*

5. Drugs:

- Corticosteroids, Thyroid hormone.
- Diazoxide, Diuretics (*Thiazides, Frusemide*).

لوا ريت جرعة زيادة لعايه

6. GESTATIONAL DM:

- IGT: first detected during LATE PREGNANCY (2nd or 3rd Tri).
- Etiology: ① IR + ② ↑ secretion of Anti - insulin hormones in late preg. *from placenta*
- Incidence: 2 % of pregnant women.

• COURSE:

- Usually: *reverts to normal after delivery.*
- In 40 %: *passes to Type 2 diabetes within 5 - 10 years.*

*تقول ده من مرض السكر
بكرت بارتفاع سوية وده يرجع طبيعي*

CLINICAL PRESENTATIONS

1. Asymptomatic: *Accidentally discovered.*
2. Symptomatic: **5 P**
 - Polyuria, Polydipsia, Polyphagia, Pruritus, Parasthesia.
 - Loss of weight: *in type 1 diabetes. ↓ insulin*
3. Complications: affecting multiple organs **or** acute complications (coma).
4. Cause: in case of secondary diabetes.

*eg: CRF
Hemochromatosis*

Oral

حوار

Q اوصف مظاهر 1 و 2 و 3 و 4

A: ② ↑ → ↓ / ① ↓

Q: ايه اللى كسر B cell في 1 و 2

A: ① by Abs / ② by Glucose toxicity

Q: هو فيه toxicity على 3 و 4

A: ① toxicity of HbA1c

Investigation

Normal

DM

FBS
Sugar

not > 110 mg/dl

IFG

impaired fasting glucose
لا يفرط

> 126

بين لازم قرائنه

2hpp

not > 140

IGT

200

75gm
جلوكوز

RBG

Random Blood sugar

> 200

بس لازم يكون

Symptomatic

fasting 115

سواء جالك متكرر

2hpp 155

مجموعة > او جالك مرة واحدة

بس واحدة (واحدة) كافية

fasting لازم متكرر

ربع المجموعة دي

25%

75%

II

محلوم

محلوم
II

لذلك لازم نقول للعلاء
follow up

DM is a laboratory diagnosis : مختبري
مختبري
diabetic

= fasting Blood glucose

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CRITERIA FOR DIAGNOSIS OF DM

1. FPG: ≥ 126 mg / dL on at least 2 separate occasions.
2. Two-hour PG: ≥ 200 mg / dL during an OGTT.
3. Symptomatic DM: plus RPG ≥ 200 mg / dL.

CRITERIA FOR DIAGNOSIS OF IFG & IGT

1. IFG: FPG is: 110 – 126 mg / dL on at least 2 separate occasions.
2. IGT: Two-hour PG is: 140 – 200 mg / dL during an OGTT.

- Both: represent a state of Hyperglycemia but do not meet the criteria for diagnosis of DM.
- Both: do not produce classic symptoms or complications of DM.
- Both: are at risk for developing Type 2 DM (25 %).

يُكتشف المرض يقول أحد ذلك أن من ضبط السكر في الدم خلال فترة ما قبل أو ما بعد الأكل يبقى هو مرض يقول أحد أكبر طالع الدم 120 يوم واحد طالع الدم مرة Zero يوم

INVESTIGATIONS

1. Plasma glucose: "Fasting & 2 hours post prandial"

- Normal levels:

- FPG: 70 – 110 mg / dL
- Two-hour PG: less than 140 mg / dL

- Abnormal levels:

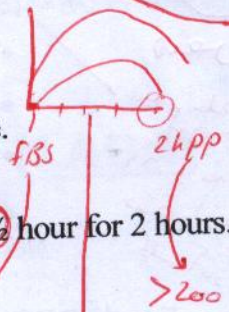
- Diagnosis of DM: see before.
- IFG & IGT: see before.

False normal of HbA1c
 ① H.A.
 ② attack hyperglycemia
 when plasma glucose is low

malabsorption
 Myxedema

2. Oral Glucose tolerance test (OGTT):

- Fasting blood & urine are collected & measured for glucose.
- The patient is given 75 gm glucose in 300 ml water orally.
- Blood & urine are collected & measured for glucose every 1/2 hour for 2 hours.



3. Urine analysis:

- To detect: glucose or acetone in urine.

4. Monitoring of treatment:

- Plasma glucose monitoring.

- Glycosylated hemoglobin (Hb-A1c):

- Formation: by linkage of glucose to β chains of Hemoglobin A.
- Value: $\frac{\text{glycated Hb}}{\text{total Hb}} \times 100$ estimates the efficiency of DIABETIC CONTROL during the preceding several weeks (6 – 12 weeks).
- Normal level: 6 % of the total hemoglobin. 15 gm average

Oral Patterns
 Urine
 Glucose acetone
 - - normal
 + -

- 1 uncontrolled DM
- 2 renal glycosuria
- 3 Hyper osmolar non ketotic

5. Investigations for:

Complications,

Cause (in secondary diabetes).

eg { CRF : RFT
 Acute MI : ECG

insulin $\rightarrow$ $\uparrow$ lipolysis $\rightarrow$ ketones
 ketones $\rightarrow$ White Knight Love

DKA = $\frac{T}{I} \frac{I}{F} \frac{F}{L}$

starvation ketosis

proper control : to delay complications but they will occur (inevitable)

الأكثر حاجة نظرياً
هو الـ ٣

COMPLICATIONS

اكتب مع Comas

I. CARDIOVASCULAR

3

1. Macrovascular complications:

"Macroangiopathy"
"Atherosclerosis"

- CAD: Angina, AMI (may be painless), HF, Sudden death.
- CVD: Stroke (cerebral thrombosis → hemiplegia).
- PAD: Ischemia of LL (intermittent claudications & gangrene).

most common cause is CAD

most common cause of nontraumatic amputation of L.L.

2. Microvascular complications:

"Microangiopathy"

- Neuropathy.
- Retinopathy. earliest
- Nephropathy. latest

والتشخيص في ١٢ سنة أو أكثر

لو جالك عندك nephro

يبقى غالباً القاعده عندك متكونه زغينه وعندك HTN

عندك تشخيص غلباً DM -> يكون بـ IGT

(multiple metabolic abnormal) = اختلالا بسموها في

3. METABOLIC SYNDROME:

"Syndrome X"

Case

- ③ HYPERTENSION. (IR of obesity)
- ② IR → HYPERGLYCEMIA (IFG or IGT or Diabetes).
- ① OBESITY, esp. abdominal (excessive fat around the abdomen).
- ④ Atherogenic DYSLIPIDEMIA (high TG, low HDL & high LDL).

early

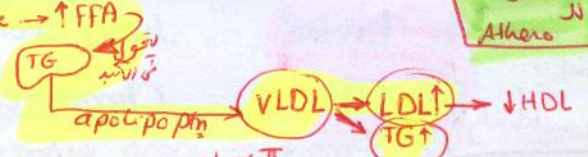
late

only in type II obese

رصد → Definition of Athero:

ATHEROSCLEROSIS IN DIABETES

- Dyslipidemia.
- Endothelial dysfunction. (due to ↑G)
- ↑ liability to HTN. (high risk)
- ↑ Cytokines → ↑ growth factors → accelerated atherosclerosis.
- Prothrombotic state: ↑ fibrinogen, vWF, PAI-1 & ↑ platelet aggregation.



oral
الخطر
LDL
والـ LDL
نوعين
large small
MW MW
↓
الخطر لانه
يسببه
تحتوي
endothelial
pores
deposited
internal
wall
رقت
plaques
عبارتي
pathology

GRF

HTN IN DIABETES

- Endothelial dysfunction. (due to ↑G) [vascular growth]
- Insulin resistance.
- Diabetic nephropathy.

rennin → RAAS

platelet clotting

Complications

DM $\rightarrow$ $\uparrow$ glucose $\rightarrow$ harmful ALL

- GEP $\leftarrow$ ① Advanced glycation end products
DAG $\leftarrow$ ② Diacyl glycerol DAG
S $\leftarrow$ ③ Sorbitol (intracellularly)
④ O_2 free radicals (oxidative stress)

Oral

(Antioxidants PO_4^{3-})
aspirin
↓ dose
↓ risk of MI
↓ Vascular Hype

DM $\hat{=}$ $\uparrow$ incidence of infection

(GRF)

- ① hyperglycemia $\Rightarrow$ good medium of infection esp $\leftarrow$ Bacterial
fungal
- ② Impaired immunity $\Rightarrow$ due to ① $\downarrow$ phagocyte fn
② $\downarrow$ neutrophil chemotaxis
- ③ Ischemia : impaired blood supply

(مخالفت اقواله انعاله هارت افعاله)

COMA, stroke ← أخطر
PN ← أسوأ

20

II. NEUROLOGICAL

4E

1. Cerebral complications: "emergencies"

- * • COMA: of different types, "see later".
- * • CVD: Stroke (cerebral thrombosis → hemiplegia).
- INFECTIONS: fungal (rhinocerebral mucormycosis).

also
aseptic
meningitis

"rare"

2. Spinal cord complications:

- Posterior column affection: Sensory ataxia.
- Pyramidal tract affection: Diabetic lateral sclerosis.

3. Root complications:

- Radiculitis: esp. affecting the roots of sciatic nerve (SCIATICA).
- Posterior root: pain & parasthesia, then, sensory loss.
- Anterior root: weakness & wasting.

Cauda equina
لأسفل
lumbosacral

4. Peripheral neuropathy:

- Refer to "neurology".

DM most common cause of PN

III. GIT

5E

↑TG → bacterial fermentation → lactic acid → demineralizes tooth enamel

1. Mouth: Dental caries, gingivitis, loosening of teeth.

2. Stomach: Gastroparesis + N, V & acute abdominal pain during DKA.

3. Intestine: Diarrhoea. [delayed gastric emptying]

4. Liver: Fatty liver. as ↑TG input in liver

5. GB: Chronic cholecystitis & gall stones are common.

- GRF
1. ↓ intest. motility (bact. overgrowth)
 2. ↑ infection incidence (infective)
 3. ± ↑ intest. motility

- Acute Abdominal in DKA
- GRF
- ① ↑ K⁺s → irritate GIT mucosa
 - ② ↑ Gastroparesis → severe abdom. distension

- ① inflammation of wall
- ② ↑ incidence of infection

- ① on top of inflammation (infection)
- ② ↑ cholesterol in blood
- ③ ↓ motility

IV. RESPIRATORY

1. INFECTIONS:

especially TB & Pneumonias.

2. During DKA:

(Breath problems)

- Rapid deep breathing (Kussmaul's breathing)
- Acetone odour in the breath. (K.B.)

Metabolic acidosis
DKA
RF

Unresolving Pneumonia
أخذ لمدة
أسبوعين ولا تحسن

لو كان فيه
Gall stone
DM
لازم
Cholecystectomy
gallstone
White Knight Love

V. GENITAL

1. Males:

Impotence.

→ autonomic neuropathy (parasymp.)
ولا أحب أدوية BB التي تزيد إفرازات
impotence

2. Females:

- Pruritus vulvae. (↑G)
- INFECTIONS: vaginal moniliasis.

DIABETES & PREGNANCY

I. Effects on DM on pregnancy:

On mother:

- Post-partum hemorrhage & puerperal sepsis.
- Premature labour, abortion, eclampsia.

On fetus:

- Congenital anomalies.
- Delivery of BIG BABIES. Macrosomia

II. Effects on pregnancy on DM:

- Gestational DM. only IGT
- Increased incidence of DKA. as pregnancy → ++ stress → ↑ant insulin

VI. OCCULAR

1. Errors of refraction.

2. Cataract.

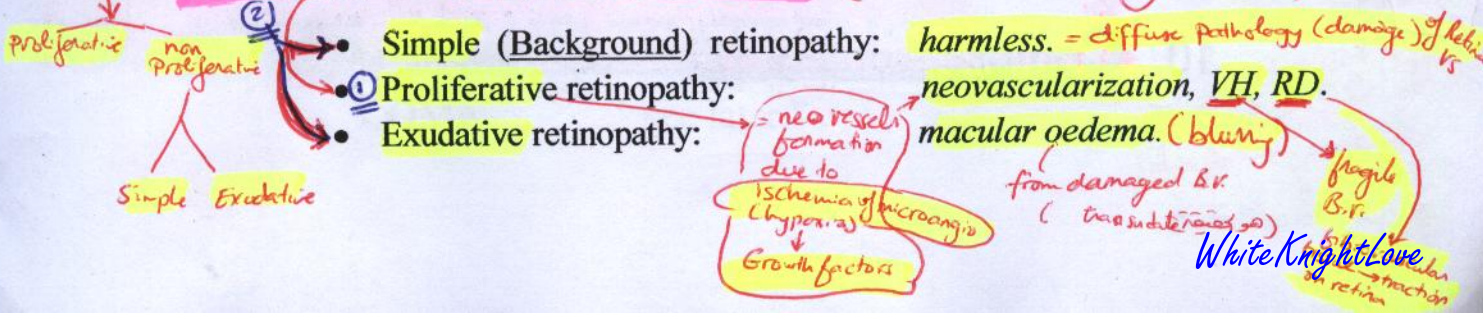
3. Glaucoma:

close angle → ↓ drainage of aqueous
due to Rubiosis iridis (new vessel formation in the iris).

4. INFECTIONS: e.g. blepharitis & panophthalmitis.

5. Nervous: paralysis of the ocular nerves, esp. 3rd nerve.

6. DIABETIC RETINOPATHY: (earliest microangiopathy in DM)



VII. CUTANEOUS

1. Pruritus:

- Especially pruritus vulvae: due to monilial infections & parasthesia.

2. INFECTIONS:

- Multiple furuncles: & carbuncles.
- Abscesses: *localized* & *diffuse* & cellulitis.
- Fungal infections: especially in the ano-genital region & interdigital.
= *toenail pedis*

3. Diabetic dermopathy:

- 1. Nature: Red painless papules.
- 2. Site: over the shins of tibiae & may ulcerate.
- 3. Cause: occlusion of the cutaneous blood vessels. → *ischemia angiodopathy* } → *rupture of extra vasation*
Clots

Painful red
erythema nodosum

4. Necrobiosis diabetorum:

- 1. Nature: Red painless papules with yellow center.
- 2. Site: over the shins of tibiae & may ulcerate.
- 3. Cause: microangiopathy & fat deposition. ↑ LDL
↑ TG

HCO
pts & acanthosis nigricans
should be screened for
Type II DM

5. Acanthosis nigricans:

- 1. Nature: Hyperpigmented (brown to black) velvety patches.
- 2. Site: over the neck, axilla or ano-genital region.
- 3. Cause: insulin spillover into the skin (due to excess insulin in IR).

DM is
Cancer stomach
Cancer Bronchus

IR → ↑ Insulin
spillover
↓ IR

MCQ People with acanthosis nigricans should be screened for diabetes

6. Delayed healing of wounds.

angiopathy

7. Xanthomata: yellow plaques around the eye lids due to hyperlipidemia.

① to ↓

② to slow down absorption

esp cholesterol

↓ absorption of fat

8. Carotinemia: yellow discolouration of skin due to ↑↑ intake of vegetables.

9. Cutaneous features of **DIABETIC FOOT**.

*color change
trophic ulcer,
gangrene*

10. Complications of ttt: e.g. insulin lipodystrophy (see ttt).

also curly

cholesterol

nephrotic
of
myxedema
DM

VIII. RENAL

1. Infections:

- Urethritis, Cystitis.
- Pyelonephritis: complicated by ACUTE NECROTIZING PAPILLITIS.

2. Stones:

- More common than in normal persons. *symptomatic or even asymptomatic*

3. Diabetic nephropathy: "Diabetic glomerulosclerosis"

1. Pathology:

- ① Thickening of the BM of the glomeruli. *IG → GF*
- ② Deposition of hyaline material (sclerosis) in the glomeruli "**KW deposits**".
- ③ Disruption of part of the membrane → excessive leak of proteins. *proteinuria*

2. Clinical picture: "Kimmelstiel – Wilson syndrome"

- ① Early: **asymptomatic** with **microalbuminuria**.
- ② Later: **persistent heavy proteinuria** & **nephrotic syndrome**.
- ③ Latest: ↓ GFR, ↑ serum creatinine & **renal failure**.

- ★ **Hypertension:** is common & it causes more renal damage.
- ★ **Diabetic retinopathy:** usually precedes the development of nephropathy.

3. Investigating:

4. Treatment:

- Early: detection of **microalbuminuria** & slowing its progression to nephropathy:

- ① Strict control of DM & HTN (120/80).

- ③ ACE inhibitors.

slow down proteinuria → ↓ progress of damage

- Later: with the onset of persistent heavy proteinuria & **nephrotic syndrome**:

- ① Strict control of DM & HTN (120/80).

- ③ ACE inhibitors or ARBs.

- ④ **Diuretics for edema**
- Latest: with development of **renal failure**:

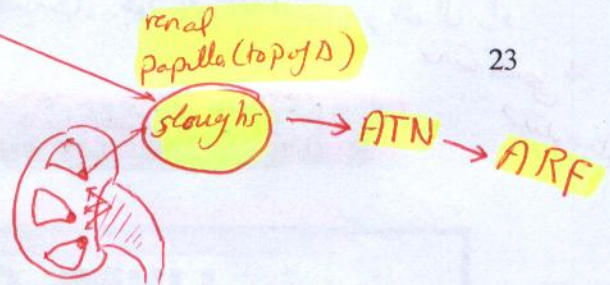
- o TTT as in uremia: renal transplantation or dialysis.

VI. ACUTE COMPLICATIONS

- COMA: "see later."

Investigating!

لا تتحوت هنا
DM في عيادة
من أي دور عدوى
صدمات الكلى
ARF
لكن هنا بالذات لأنه فيه
Angiopathy & ischemia



SCQ
Case

DM في عيادة
لا بد من فحص
screening for
microalbuminuria

Criteria
nephrotic
RF
Criteria

renal damage
aggravated by
1. HTN
2. HTN
3. proteinuria
(damage effect on tubules)

normally
maybe traces
of albumin in urine
24 hours
Omg till to 1 or 2
upto 150/day
no less
150/d
2 < 300/d
asymptomatic
300
nephrotic
(heavy proteinuria)
upto
> 3500
14,000
14,000
gm

أوعي نكتب
nephrotic
control
لأنه الكلى ترفض
idiopathic nephrotic
Diabetic nephrotic
White Knight Love

ماتت السخى و
ويقلوه ماء

TREATMENT OF DM

LINES OF TREATMENT

- I. DIET TREATMENT.
- II. ORAL HYPOGLYCEMIC DRUGS.
- III. INSULIN.
- IV. NEW LINES OF TTT.
- V. TTT OF COMPLICATIONS.
- VI. TTT OF THE CAUSE.
- VII. TTT OF SPECIAL SITUATIONS.

I. DIET TREATMENT

CONCEPT

- To keep caloric supply in a range compatible with endogenous insulin.

CALCULATION OF DAILY CALORIES

- For underweight patients: 40 cal / Kg / day.
- For average weight patients: 30 cal / Kg / day.
- For overweight patients: 20 cal / Kg / day.

CHOICE OF DAILY CALORIES

- Carbohydrates: 50 % of calories.
- Fats: 30 % of calories.
- Proteins: 20 % of calories.

CHOICE OF CARBOHYDRATES

- Avoid simple sugars: because they are rapidly absorbed.
- Allow complex sugars: because they are slowly absorbed.

CHOICE OF MEALS

- 1 ○ Advise food rich in fibres (e.g. bran), because fibres will slow sugar absorption.
- 2 ○ Advise frequent small meals:
 - To avoid hypoglycemic attacks with insulin & oral ttt.
 - To avoid hyperglycemic peaks with large meals.

Breakfast

Lunch

Dinner

not heavy to avoid ↓G

Snack to avoid ↓G

II. ORAL HYPOGLYCEMIC DRUGS

1. Sulphonylureas

"Insulin secretagogues"

1 ACTION

- Decrease insulin resistance.
- Increase insulin secretion from the pancreas: **MAIN ACTION.**
- Decrease hepatic glucose production.

exhausted B cell → لا بد فزة مؤجلة → ١ قلب

insulin secretagogue

2 INDICATIONS

- NIDDM: **not** controlled on diet ttt.

3 CONTRAINDICATIONS

- IDDM.
- NIDDM: with severe hyperglycemia. → ١ قلب
- DKA.
- Diabetes with pregnancy. Teratogenic → ١ II v. late
- Surgery.
- Severe liver disease or renal disease.

indications of insulin

anticoag. & preg (teratogenic)

الى م. محذوف insulin خاص

4 PREPARATIONS

Drugs	Daily dose in mg	Duration of action, hours
First generation drugs		
Chlorpropamide	100 - 500	24 - 48
Tolazamide	100 - 1000	12 - 24
Tolbutamide	500 - 3000	6 - 12
Second generation drugs		
Glimepride	1 - 8	24
Glibenclamide	5 - 15	12
Glipizide	2.5 - 40	12
Gliclazide	80 - 320	12

recent short acting

NB Second generation drugs are preferred because of shorter duration of action and therefore **less incidence of hypoglycemia.**

5 SIDE EFFECTS

- HYPOGLYCEMIA:**
- BM: depression,
- GIT: irritation.
- Skin: rash.

especially with first generation drugs.
especially with Chlorpropamide.

Aplastic anaemia

↓ G side effect
اكثر مع oral
مع insulin

NO side effect of IG

26

2. Biguanides

1 ACTION

- Increase: passage of glucose into the cells.
- Increase: anaerobic glycolysis.

- Decrease: appetite.
- Decrease: glucose absorption.
- Decrease: gluconeogenesis.

NOT insulin secretagogues

side effect → Lactic Acidosis

2 INDICATIONS

- Obese NIDDM (Type II B): (80%) not controlled on diet ttt.

3 CONTRAINDICATIONS

- Same as: Sulphonylureas.

4 PREPARATIONS

- Metformin: 500 mg tds. ^{x3}
- Phenformin: 25 mg tds (not used now). as severe lactic acidosis & may be coma

5 SIDE EFFECTS

- Appetite: loss.
- GIT: irritation. V. severe →
- Lactic acidosis. ^{anaerobic}
- Homocysteinemia. ^{low risk of atherosclerosis}
- Anemia: due to vitamin B12 malabsorption.
- ALONE: THEY DO NOT CAUSE HYPOGLYCEMIA.

أولى قبل الأكل
لازم بعد الأكل
خطا شائع أروسة

3. New oral hypoglycemic drugs

Complex sugar
α-glucosidase
Simple sugar

- a) Alpha - Glucosidase inhibitors: e.g. Acarbose.
- Decrease post prandial hyperglycemia by: delaying glucose absorption.

- b) Benzoic acid derivatives: e.g. Repaglinide.
- Increase INSULIN SECRETION. V. potent secretagogue

- c) Insulin sensitizers: "Thiazolidine-diones" e.g. Rosiglitazone & Pioglitazone.
- Decrease INSULIN RESISTANCE (PPARγ agonists).

PPAR-γ
Peroxisome
Proliferator
Activated
Receptor
= receptor molecules intracellular (nuclear)
this drugs binds to them

- ① upregulate insulin receptors (S.U.)
- ② improves intracellular enzymatic Rx (post receptor)

P PPAR Gamma

White Knight Love

III. INSULIN

INDICATIONS

- **IDDM.**
- **NIDDM:** with severe hyperglycemia not controlled by diet & OHD.
- **DKA.**
- **Diabetes with pregnancy.**
- **Surgery.**
- **Severe liver disease or renal disease.**
- **Severe stress:** infection. *due to anti-insulin release*

سؤال عام
= clinical uses = indications + Hyperkalemia
أكبر استخدامات

ORIGIN

- Animal insulin: from cows or pigs rarely used now.
- Human insulin: genetic engineering widespread use now:
most powerful, least allergic.

obsolete
cheap

insulin up → ↑ incidence of insulin resistance

PREPARATIONS

Insulin	Onset	Peak	Duration
Short acting			
Crystalline (regular)	½	3	6
Semilente	1	6	12
Intermediate acting			
Isophane (NPH)	3	8	24
Lente	3	8	24
Long acting			
Protamine zinc insulin	4	16	36
Ultralente	4	16	36
Mixtures	Mixtard: 30 / 70 & Initard: 50 / 50		

- ① Brittle (fluctuant)
- ② Newly diagnosed hyperglycemic pt
- ③ Diabetic Coma or hyperosmotic Coma
- ④ Surgery

(no incidence of insulin resistance)

pt poorly controlled

oral

قاعدة

short:

is used

when DM

is poorly

controlled

التي

short

max 24h

لا

dinner

lunch

breakfast

لا يتغير مع الوقت فقط لقاعدة 24 ساعة
Short X long

DOSE

- The ttt is usually started with 20 units / day in average weight patients.
- The dose is gradually increased (e.g. by 5 - 10 units / day) until blood glucose is controlled.
- The dose is maintained for life & monitored

لأنه الجسم قابلية للتغير حسب لوتدهور أو نقص

طاقة تحت أن

every 3w

every 3M

Blood glucose

glycated HbA1c

by daily

Blood glucose

6 times / d

قبل وجبة أو وجبات

not by HbA1c

لا يتغير مع الوقت فقط لقاعدة 24 ساعة

White Knight Love

ADMINISTRATION

A SUBCUTANEOUS:

Many methods could be used, e.g.

1. Single injection before breakfast:

"Mixtard"

- Short acting (30 % of the required dose) + long acting (70 % of the required dose).

2. Twice daily injections:

"Long"

- Morning injection: $\frac{2}{3}$ of the total daily dose.
- Evening injection: $\frac{1}{3}$ of the total daily dose.

eg 60 units
 $\frac{2}{3}$ every
 $\frac{1}{3}$ every

3. Multiple daily injections: "in cases of poor glycemic control"

- Regular insulin before each meal + evening long acting insulin.

NB Injections can be given by insulin syringes or by pen injection devices.

قلم وحقنة من الأنسولين وحقن الودعات بغير حقنة وحقنة

- 1. Economical
- 2. Painless
- 3. Used by blind PT (Retinopathy)

4. Continuous Subcutaneous Insulin Infusion:

Insulin pump

They deliver: **rapid-onset, short-acting insulin** 24 hours a day,
 Through a: **catheter placed under the skin.**

DOSES:

- **Basal** (small) dose: delivered constantly.
- **Bolus** dose: delivered with meals.

ADVANTAGES:

- Eliminates the need for injections.
- Delivers insulin more accurately than injections.
- Decreases the fluctuations in blood glucose levels.
- Decreases the episodes of hypoglycemia.
- Allows more flexibility with meals.

DISADVANTAGES:

- Expensive.
- Inconvenient.
- DKA: if the catheter comes out & there is no insulin for hours.

B IV infusion or IM:

In case of DKA or Hyperosmolar coma.

C Insulin spray (Nasal or Oral):

New.

D Oral insulin:

Investigational.
 as its bioavailability by GIT (nil)

Oral
 anti-insulin
 كثير الصبح
 معانزها قليلة بالليل
 خاف من nocturnal hypoglycemia

Break Launch Dinner
 ↑ ↑ ↑
 S S S
 Long
 لقاح ثنائي يومه الصبح



جهاز
 وقعة
 قسطرة
 تحت الجلد

اختاروها
 في
 insulin
 الصبح
 اللوحه يطولهم
 البكر ياتي د
 2 patterns
 basal & pulsatile
 فيزونه وجه مؤكل
 معانه يولد
 في Glycemia

لحمه فيه
 basal insulin
 اما الحقنه في ندى جوده والجسم يقلل
 rebound by anti-insulin

مكتفاه لما ياخذ دس لازم يحوت
 DKA لو ناموا اخلت

COMPLICATIONS

1. HYPOGLYCEMIA.

2. Weight gain. $E \begin{cases} \uparrow \text{lipogenesis} \\ \downarrow \text{lipolysis} \\ \uparrow \text{appetite} \end{cases}$

3. Insulin lipodystrophy: atrophy of SC fat at sites of injections forming skin dimples.

4. Allergic reactions: least with human insulin. $\uparrow$ animal

5. Insulin resistance: due to:

- Antibodies against insulin preparations (least with human insulin). $\uparrow$ animal
- Obesity. $++$ fat cells $\rightarrow ++$ IR $\rightarrow$ احتياج جرعات أكبر $\rightarrow$ على المدى الطويل $\rightarrow$ Oral

6. Insulin in a wrong dose: "Night Dose"

- Dawn phenomenon: morning hyperglycemia due to under dosage of insulin.
- Somogyi effect: morning hyperglycemia following nocturnal hypoglycemia due to over dosage of insulin.

HONEYMOON PHASE

- A TEMPORARY phase in the first 1 – 2 years after the onset of TYPE I DM.
- Reduction in exogenous insulin needs due to temporary improvement in β cell function.
- Blood glucose is controlled with very small doses of insulin.

IV. NEW LINES OF TTT

- Pancreatic transplantation.
- Pancreatic islet cells transplantation.

V. TTT OF COMPLICATIONS

chronic e.g. TTT of diabetic nephropathy: see before.

acute e.g. TTT of different types of coma: see later.

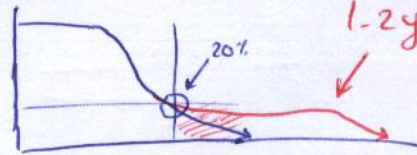
DICA

VI. TTT OF CAUSE (in secondary D)

e.g. TTT of CRF.

diagnosis

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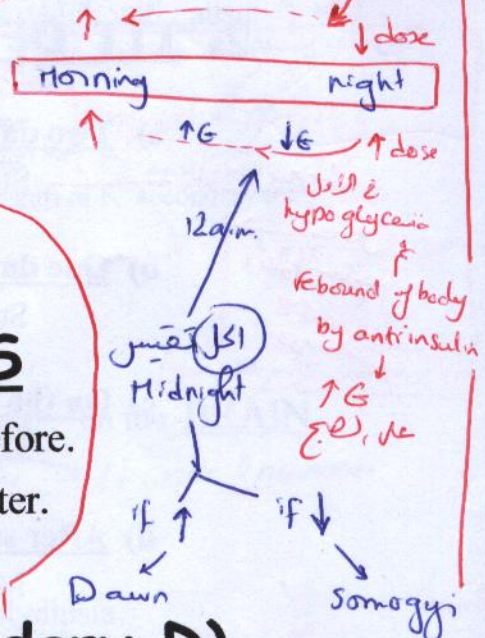


normal course of type 1
1-2 years stability
بدل ما ينزل
steeping
29
بدراسة
ساعات تحصل
أفضل سوية
خضر

خطأ
٢٢ جيد الدكتور
under

لم تنزود
المجرعة على
المدى

Oral



↑ dose
↓ dose
↑G
↓G
12 a.m.
hypo glycaemia
↑ rebound of body
by antrinsulin
↑G
على العلاج

اكل تقيس
Midnight

Dawn

Somogyi

وتقول طابا انه
يبقى معكم تنزود جرعة بالليل
لانه معكم يكون
وانت مستعاطان
تنزود المجرعة عما هو زائدة اهدا
White Knight Love

VII. TTT OF SPECIAL SITUATIONS

1. TTT OF DM DURING PREGNANCY

SQ

a) General:

Daily home blood glucose monitoring + outclinic assessment every 2 weeks.

b) Investigations:

Fundus exam. + urinary protein at first, at 28 weeks & before delivery, because *retinopathy* & *nephropathy* may deteriorate during pregnancy.

(eclampsia)
is predisposed by DM

c) Control:

By diet ttt, if not enough, give insulin.

Oral hypoglycemic drugs are contraindicated.

Teratogenic
Antistress

SQ

2. TTT OF DM DURING SURGERY

لوعلى
cholecystitis
DM

لازم جراح و اعلى

a) Two days before surgery:

Stop: oral hypoglycemic drugs.

لو هو مبروت

b) One day before surgery:

Stop: long acting insulin & replace by: short acting insulin.

✓

c) On the surgery day:

Give: infusion of glucose, short acting insulin & K.

as ↓ K
anhydrosis

d) After surgery:

Maintain: the infusion until the patient is allowed to eat.

e) Monitoring:

Check: glucose & K levels every 4 hours.

intra & post opent

تم ترجيع العلاج الى كانه مايش عليه قبل الجراح

إندوكرين
endocrine

COMA IN DM

I. DIABETIC KETOACIDOSIS (DKA)

"Diabetic coma"
Acute condition
on top of chronic

- DKA is the hallmark of TYPE I DM. (DKA prone)

ETIOLOGY

- **Stoppage of insulin intake** (missed insulin). *adequate but ↑ G diet*
- **Severe hyperglycemia** (inadequate tt). *inadequate from start*
- **Stress of a precipitating factor:** *which needs high energy as in:*
 - Psychological stress.
 - Pregnancy, labour.
 - Stroke, AMI.
 - Surgery, Infection, Trauma.

antinsulin!!

PATHOGENESIS

(absolute insulin deficiency)

1. Insulin: very low → hyperglycemia → osmotic diuresis → **Dehydration**.

2. Fats: Lipolysis to produce energy → ↑↑ ketone bodies which will cause:

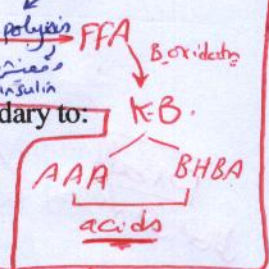
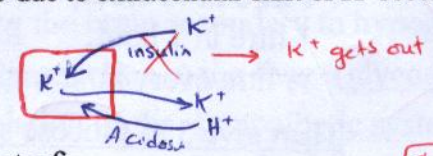
- Ketonemia → **Metabolic acidosis**.
- Ketonuria → acetone in urine.

ربط بين السكر و ketone

3. Potassium: **Hyperkalemia** occurs due to extracellular shift of K secondary to:

- Insulin deficiency.
- Acidosis.

oral normal total body K or low if severe osmotic diuresis



4. COMA: due to the combined effect of:

Dehydration, Acidosis, & Hyperkalemia: on the **BRAIN**.

shrinkage (hypertonic) encephalopathy → ↓ cortical neurones

CLINICAL PICTURE

1. General: Slow onset with marked Polyuria + Polydipsia. *hours to days*
2. GIT: Dyspepsia, nausea, vomiting, + acute abdominal pain. *asymptomatic*
3. Breath: Rapid deep breathing (Kussmaul's) + acetone odour.
4. Brain: Confusion, then Coma. (dehydrate, Acidosis, HyperK⁺)
5. Dehydration: Dry skin, dry tongue, sunken eyes, + weak rapid pulse, ↓ BP. *hypovolemic shock*

hypoglycemia (minutes)

hypoglycemia عرقانة

WhiteKnightLove

Q Management DKA : Pathogens / CIP / investig / ttt
(25M) then after control of DKA DM علاج DM

(Contra indication) Diet . Insulin . لو كبت oral hypoglyc

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INVESTIGATIONS

1. Blood: Glucose is markedly increased.
2. Urine: Glucose & acetone appear in urine. → DKA
3. Serum K: Increased (extracellular shift).
4. pH: Decreased. $\bar{e}$ Total body K either Normal or ↓ if severe osmotic diuresis
5. Serum Na: HCO_3^- ↓ (arterial) Increased due to concentration by dehydration

TREATMENT

1. HOSPITALIZATION:

better in an ICU.

2. INSULIN:

- Type: short acting insulin.
- Route:
 - During ketosis: $\rightarrow$ steady control
 - After disappearance of ketosis: Multiple daily SC injections.
- Dose:
 - 6 – 10 units / hour: until ketosis disappear.
 - Larger doses (12 – 20 units / hour): may be used in resistant cases.

3. IV FLUIDS:

- Amount required: usually 4 – 8 litres.
- Type:

Start by normal saline as follows:

- 1 litre in $\frac{1}{2}$ hour, followed by:
- 1 litre in 1 hour, followed by:
- $\frac{1}{2}$ litre every hour until the deficit is replaced.

Then give 5 % glucose solution:

When blood glucose drops to 250 mg / dl: to avoid hypoglycemia.

4. CORRECTION OF ACIDOSIS:

- IV infusion of sodium bicarbonate: in severe acidosis (pH < 7.1).
[if HCO_3^- ↓ < 10 mEq/L]

5. POTASSIUM:

Should be given because:

- Hypokalemia occurs during ttt due to intracellular shift of K secondary to:
 - Insulin therapy.
 - Correction of Acidosis.
- Dose: 20 – 40 mEq of K added to each litre of infusion.

White Knight Love
guided by serum K

6. TTT OF THE PRECIPITATING FACTORS:

- e.g. Antibiotics for infection.

7. MONITORING OF THE PATIENT

• Clinically:

- Level of consciousness. → Glasgow Coma Scale
- Signs of dehydration.
- PULSE, BP & CVP. إم حارة

• Laboratory:

- Blood: Glucose.
- Urine: Glucose & acetone.
- Serum K.
- pH.

II. HYPOGLYCEMIC COMA

ETIOLOGY

- Over dose of insulin or sulphonylurea.
- Diminished carbohydrate intake following ttt: missed meal.

Not Biguanides as not secretagogues

PATHOGENESIS

- Coma: due to ↓ energy supply to the brain secondary to hypoglycemia.
- Adrenaline: is secreted to ↑ glucose production in the liver (glycogenolysis).
- Hyperadrenalism: occurs & causes stimulation of the sympathetic system.
↑ catecholamines

CLINICAL PICTURE

- There are features of:

“Sympathetic over activity”

- Symptoms: Rapid onset of Irritability, tremors, pallor, sweating, palpitation.
- Signs: Dilated pupils, moist skin, strong rapid pulse, ↑ BP.
- Course: Convulsions, Coma, Brain damage & death in severe cases.
- Response to ttt: Rapid response to IV or oral glucose.

Sympathetic

brain death حالة حادة قبل

لوحظت
تغيرت عليه

أو ما يسمى
بالحرمة
والرعدة

كثرة

DKA
Slow

DKA
Sunken eye
dry
weak
↓ BP

INVESTIGATIONS

1. Blood: Glucose is markedly decreased ($< 50 \text{ mg / dl}$).
2. Urine: No glucose in urine.

TREATMENT

1. In severe hypoglycemia: IV glucose & IV glucagon (in resistant cases).
2. In early hypoglycemia: oral glucose.

antinsulin → ~~glycogenolysis~~ → ++ Glucose

	DKA	Hypoglycemia
1. History	Missed insulin	Missed meal
2. Onset	Slow	Rapid
3. Coma	Silent	Irritable
4. Skin	Dry	Moist
5. Tongue	Dry	Moist
6. Eyes	Sunken	Normal
7. Pupils	Normal	Dilated
8. Respiration	Kussmaul's	Normal
9. Breath	Acetone odour	Normal
10. Pulse	Weak & rapid	Strong
11. BP	Low	High
12. Urine	Glucose & acetone	Normal
13. Blood glucose	Very high	Low
14. Response to glucose	No effect	Rapid improvement

لو واحد ز العرا وعنده غيبوبة و ساطع

مبدأ ادى جلوكوز

لأنه لو كانه $\downarrow G \rightarrow$ غيبوبة
ولو كانه DKA $\leftarrow 1000$ من غيبوبة معاه

Relative Insulin Deficiency

35

III. HYPEROSMOLAR NON-KETOTIC COMA

Severe hyperglycemia without ketosis, usually in a neglected elderly TYPE 2 DM.

ETIOLOGY

1. Uncontrolled Type 2 DM: with severe hyperglycemia.
2. A precipitating factor such as: Stroke, AMI, or infection.

PATHOGENESIS

1. Insulin deficiency is less severe in Hyperosmolar coma than in DKA.
2. Low endogenous insulin → hyperglycemia → osmotic diuresis → Dehydration.
3. Low endogenous insulin: is sufficient to inhibit ketogenesis → no Acidosis.

Concentrated Na
Hyper osmolar

CLINICAL PICTURE

"Dehydration with no acidosis"

1. General: Slow onset with marked Polyuria + Polydipsia.
2. Brain: Confusion, then Coma. (due to dehydration only not Acidosis)
3. Dehydration: Dry skin, dry tongue, sunken eyes, + weak rapid pulse, ↓ BP.

no GIT / no

INVESTIGATIONS

1. Blood: Glucose is markedly increased, ↑ Na (due to dehydration).
2. Urine: Glucose appears in urine, BUT no acetone.

TREATMENT

1. Hospitalization: better in an ICU.
2. IV fluids: using normal saline
3. Insulin: as in DKA.
4. Potassium: as in DKA.
5. Na Bicarbonate: is not given.
6. TTT OF THE PRECIPITATING FACTORS: e.g. Antibiotics for infection.
7. Monitoring the patient: as in DKA.

"The most important measure"

no add fluids to normal saline
insulin 2 units/hr

no need for pH monitoring as no ~~D~~ Acidosis

IV. LACTIC ACIDOSIS COMA

حتى لو اسكر
عنا

ETIOLOGY

- It occurs in diabetics using **BIGUANIDES**.
- It may be precipitated by **TISSUE HYPOXIA**, e.g. **HF** (shock, resp. failure).
- BIGUANIDES** or **TISSUE HYPOXIA** → Anaerobic glycolysis.
- Anaerobic glycolysis → accumulation of lactic acid → severe **Acidosis**.

anaerobic → L.A.
Pyruvic acid

و طوائف
benfennit

ppt by DM

CLINICAL PICTURE

"Acidosis with no dehydration"

- Breath:** Rapid deep breathing (Kussmaul's) ~~acetone odor~~ PH ↓
- Brain:** Confusion, then Coma.

Investig: ↓PH

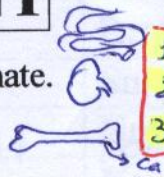
TREATMENT

- IV sodium bicarbonate.

Hyperparathyroidism
is not the only cause of PTH

PTH ↓ serum P
↑ serum Ca

control
vit D
so, ↓ serum Ca



- intestine: ↑ absorption (act. vit D)
- Kidney: ↑ reabsorption, & ↑ excretion of P
- Bone: ↑ resorption (osteoclastic activity)

* functions of Ca:

- Mus contraction (actin over myosin)
- Neuromuscular transmission
- Bone & teeth
- Coagulation system

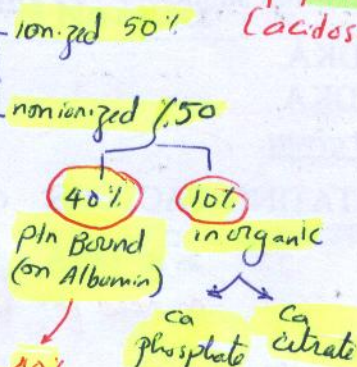
* Normal Levels

total Ca : 8.5 - 10.5 mg/dl
P : 2.5 - 4.5 mg/dl

- * ↑ Ca & ↑ P = Acromegaly
- * ↓ Ca & ↓ P = malabsorption

نمنا كذا الحيات الرقتل
ده تزود ده العكس

albumin ضروري
nephrotic syndrome
serum Ca normal
also Albumin must be normal



if pH normal 50% ionized
50% non "

if pH ↑ (alkalosis) ionized ↓
if pH ↓ (acidosis) ionized ↑

pH
ماتوس مائة
total
(لاغير)

shift فقط
ionized
& non "

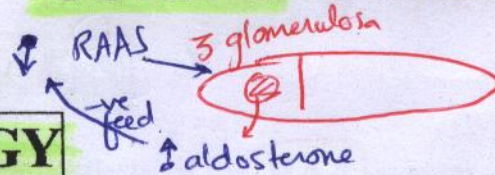
IBD, DM, parathyroid
→ Kidney stones

PRIMARY HYPERALDOSTERONISM SP

"CONN'S SYNDROME"

ETIOLOGY

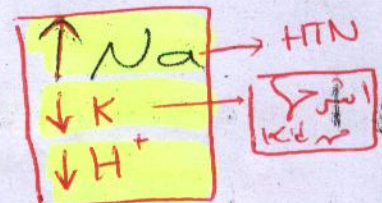
1. Adrenal adenoma: the most common cause.
2. Adrenal hyperplasia: bilaterally.



*↑ aldosterone
↓ renin activity by
-ve feedback.*

CLINICAL PICTURE

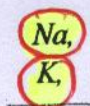
1. Hypertension: may be severe & malignant.
2. Hypokalemia: see "kidney".
3. Metabolic alkalosis: see "kidney".
4. Polyuria: *hypokalemia - sensitivity of renal tubule to effect of ADH*



INVESTIGATIONS

1. Blood Chemistry:

- Increased:
- Decreased:



due to metabolic alkalosis

HCO₃⁻

Aldosterone

Plasma rennin activity

-ve feed

2. Imaging:

- CT & MRI: abdomen will differentiate between adrenal tumours & hyperplasia.

3. ECG:

- Evidence of Hypokalemia: see "Kidney".

TREATMENT

1. For adenoma: surgical removal.
2. For hyperplasia: spironolactone 100 - 400 mg daily (K - sparing diuretic).

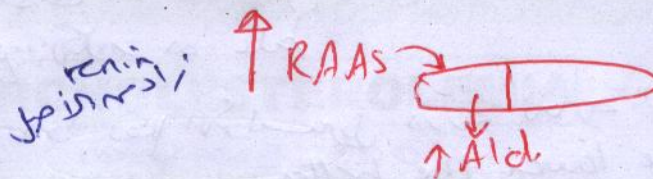
*aldosterone antagonist
& treats also HTN] double effect.*

SECONDARY HYPERALDOSTERONISM

SP

1 DEFINITION

- It is an increased activity of the **RAA** system.



2 ETIOLOGY

Renin overproduction:

- Accelerated & Malignant hypertension.
- Renal artery stenosis.

renal damage
renal ischaemia
hypoxia

↑ renin

Hypovolemia:

- Heart failure.
- Liver failure.
- Nephrotic syndrome.
- Excess diuretics.

renal hypoxia

Extravascular edema
volume ↓ B.V. → GFR ↓

3 C/P as 1ry hyperaldosteronism (Conn's)

4 INVESTIGATIONS

- Increased: Plasma rennin activity, Plasma Aldosterone.
- Serum Na: may be low in cases of Hypovolemia.

Conn's
(↓)

↑ ACTH
Cushing's

5 TREATMENT

- ACE inhibitors.
- Spironolactone. aldosterone antagonist
- TTT of the cause. eg H.f. : digitalis

stop renin
stop Aldosterone

Oral 1000

63

DISORDERS OF LIPID METABOLISM

N: 150-200 mg/dl

normally cholesterol not more than

HYPERCHOLESTEROLEMIA

200 mg/dl

1. Primary:may reach 1000
Familial Hypercholesterolemia (FH).

→ most common cause of stroke & coronary in young age

2. Secondary:

- Hypothyroidism.
- Obstructive jaundice. *normal esterification*
- Nephrotic syndrome.
- Acute intermittent porphyria. *inborn error in haeme metabolism*
- DRUGS: *Thiazide diuretics, Cyclosporine. @ associated inborn error in lipid metabolism*

HYPOCHOLESTEROLEMIA

1. Malnutrition, Malabsorption.

2. Hyperthyroidism.

3. Chronic infections:

*AIDS, TB.**Catabolic on cholesterol***HYPERTRIGLYCERIDEMIA**

1. Metabolic:

*DM**CRF.**→ the most common cause.*

2. Obesity.

3. Alcoholism.

*→ apolipoprotein inhibition*4. DRUGS:*Thiazide diuretics,**Estrogen,**Beta adrenergic blockers.***COMBINED HYPERLIPIDEMIA**

1. Hypothyroidism.

2. Nephrotic syndrome.

3. Thiazide diuretics.

• ↑ cholesterol dangers: { Brain
heart
B.V.

• ↓ cholesterol: زمان كانوا فاكرين له خطورة
{ ↑ incidence cancer
psychiatric disturbance
دلو قى طلع الكلاء ده غلام

لذلك لما ندى دوا يقل الكوليسترول ندره لغاية اى ندى؟
the lower the better

• ttt for ↑ cholesterol:

- Statins * ↓ HMG Co-A Reductase
Hydroxy Methyl Glutaryl
so, ↓ synthesis of cholesterol

* side effect: - on H.S & liver
- compensatory ↑ in ^{absorption} synthesis

- Ezetimibe: * ↓ absorption
* side effect - compensatory ↑ in synthesis

statin + Ezetimibe
in v. severe ↑ cholesterol

دوا اى
Inegy → avoids compensatory rise

صالح
معالجته

• ttt for ↑ TG:

- Fibrates

• ttt for combined → Ch: 400
TG: 1600 زيغنا

fibrates (مع) statin
or Inegy لا ينفج اى

والا ضايع ال liver

الكل اعلاج واحد وبعده واحد

اعلاج من الاول؟ مبعأ

Oral 1000

TG النعل

الهدف من علاج اى افعل
LDL
N: 130 mg/dl
عائز نزل عن 130
واذا الناس high risk
عائز نزل عن 100
و recently
قله الى 70

لانه هو العيان من هيجل stroke الزرارة
TG نعل حاب acute

Hypertiglyceridemia → Acute pancreatitis

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TG و يجرش حابه (cholesterol) سببه مؤقتاً سون